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(54) **Quinoline derivatives as tachykinin NK3 receptor antagonists**

Chinolinderivate als Tachykinin NK3 Rezeptor Antagonisten

Dérivés de quinoléine en tant qu'antagonistes du récepteur de tachykinine NK3

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(56) References cited:
- **BRIAN J. WILLIAMS ET AL.: "Cyclic peptides as selective tachykinin antagonists." JOURNAL OF MEDICINAL CHEMISTRY., vol. 36, no. 1, - 8 January 1993 AMERICAN CHEMICAL SOCIETY. WASHINGTON., US, pages 2-10, XP002114220**

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Description

[0001] The present invention relates to novel quinoline derivatives, processes for their preparation and their use in medicine.

[0002] The mammalian peptide Neurokinin B (NKB) belongs to the Tachykinin (TK) peptide family which also include Substance P (SP) and Neurokinin A (NKA). Pharmacological and molecular biological evidence has shown the existence of three subtypes of TK receptor (NK_1, NK_2 and NK_3) and NKB binds preferentially to the NK_3 receptor although it also recognises the other two receptors with lower affinity (Maggi et al, **1993**, *J. Auton. Pharmacol.*, *13,* 23-93).

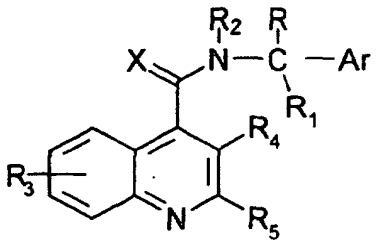
[0003] Selective peptidic NK_3 receptor antagonists are known (Drapeau, **1990** *Regul. Pept.*, 31, 125-135), and findings with peptidic NK_3 receptor agonists suggest that NKB, by activating the NK_3 receptor, has a key role in the modulation of neural input in airways, skin, spinal cord and nigro-striatal pathways (Myers and Undem, 1993, J.Phisiol., 470, 665-679; Counture et al., 1993, Regul. Peptides, 46, 426-429; Mccarson and Krause, 1994, J. Neurosci., 14 (2), 712-720; Arenas et al. 1991, J.Neurosci., 11, 2332-8).

[0004] However, the peptide-like nature of the known antagonists makes them likely to be too labile from a metabolic point of view to serve as practical therapeutic agents.

[0005] We have now discovered a novel class of selective, non-peptide NK_3 antagonists which are far more stable from a metabolic point of view than the known peptidic NK_3 receptor antagonists and are of potential therapeutic utility in treating pulmonary disorders (asthma, chronic obstructive pulmonary diseases -COPD-, airway hyperreactivity, cough), skin disorders and itch (for example, atopic dermatitis and cutaneous wheal and flare), neurogenic inflammation and CNS disorders (Parkinson's disease, movement disorders, anxiety and psychosis). These disorders are referred to hereinafter as the Primary Disorders.

The novel NK_3 antagonists of the present invention are also of potential therapeutic utility in treating convulsive disorders (for example epilepsy), renal disorders, urinary incontinence, ocular inflammation, inflammatory pain, eating disorders (food intake inhibition), allergic rhinitis, neurodegenerative disorders (for example Alzheimer's disease), psoriasis, Huntington's disease, and depression (hereinafter referred to as the Secondary Disorders).

[0006] According to the present invention there is provided a compound, or a solvate or salt thereof, of formula (I):



(I)

Wherein, Ar is phenyl, 2-chlorophenyl, 2-thienyl or cyclohexadienyl;

R is methyl, ethyl, n-propyl, -COOMe, -COMe;

R_1 and R_2 are each hydrogen or methyl;

R_3 is hydrogen, methoxy, or hydroxy;

R_4 is hydrogen, methyl, ethyl, methoxy, hydroxy, amino, chlorine, bromine, dimethylaminoethoxy, 2-(1-phthaloyl) ethoxy, aminoethoxy, 2-(1-pyrrolidinyl)ethoxy, dimethylaminopropoxy, dimethylaminoacetylamino, acetylamino, and dimethylaminomethyl.

R_5 is phenyl, 2-thienyl, 2-furyl, 2-pyrryl, 2-thiazolyl and 3-thienyl;

and X is oxygen;

[0007] With the priviso that said compound of formula(I) is not N-(α-ethylbenzyl)-3-hydroxy-2-phenylquinoline-4-carboxamide.

[0008] The compounds of formula (I) or their salts or solvates are preferably in pharmaceutically acceptable or substantially pure form. By pharmaceutically acceptable form is meant, inter alia, of a pharmaceutically acceptable level of purity excluding normal pharmaceutical additives such as diluents and carriers, and including no material considered toxic at normal dosage levels.

A substantially pure form will generally contain at least 50% (excluding normal pharmaceutical additives), preferably 75%, more preferably 90% and still more preferably 95% of the compound of formula (I) or its salt or solvate.

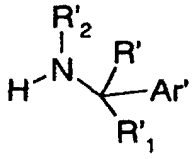
One preferred pharmaceutically acceptable form is the crystalline form, including such form in pharmaceutical composition. In the case of salts and solvates the additional ionic and solvent moieties must also be non-toxic.

[0009] Examples of pharmaceutically acceptable salts of a compound of formula (I) include the acid addition salts with the conventional pharmaceutical acids, for example maleic, hydrochloric, hydrobromic, phosphoric, acetic, fumaric, salicylic, citric, lactic, mandelic, tartaric, succinic, benzoic, ascorbic, and methanesulphonic.

[0010] Examples of pharmaceutically acceptable solvates of a compound of formula (I) include hydrates.

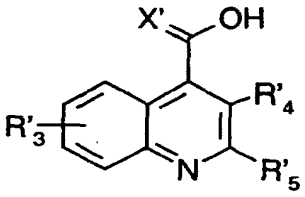
[0011] The compounds of formula (I) may have at least one asymmetric centre and therefore may exist in more than one stereoisomeric form. The invention extends to all such forms and to mixtures thereof, including racemates.

[0012] The invention also provides a process for the preparation of a compound of formula (I) which comprises reacting a compound of formula (III)



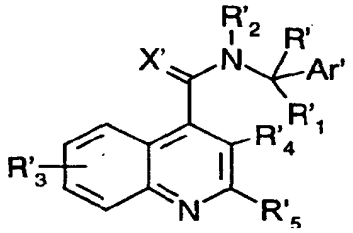
(III)

in which R', R'_1, R'_2 and Ar' are R, R_1, R_2 and Ar as defined for formula (I) or a group or atom convertible to R, R_1, R_2 and Ar, with a compound of formula (II)



(II)

or an active derivative thereof, in which R'_3, R'_4, R'_5 and X' are R_3, R_4, R_5 and X as defined for formula (I) or a group convertible to R_3, R_4, R_5 and X, to form a compound of formula (Ic)



(Ic)

and optionally thereafter performing one or more of the following steps:

(a) where R', R'_1 to R'_5, Ar' and X' are other than R, R_1 to R_5, Ar and X, converting any one of R', R'_1 to R'_5, Ar' and X' to R, R_1 to R_5, Ar and X to obtain a compound of formula (I),
(b) where R', R'_1 to R'_5, Ar' and X' are R, R_1 to R_5, Ar and X, converting any one of R, R_1 to R_5, Ar and X to another R, R_1 to R_5, Ar and X, to obtain a compound of formula (I),
(c) forming a salt and/or solvate of the obtained compound of formula (Ic).

[0013] Suitable active derivatives of the compounds of formula (II) are acid halides (preferably chlorides), acid azides or acid anhydrides. Another suitable derivative is a mixed anhydride formed between the acid and an alkyl chlorofor-

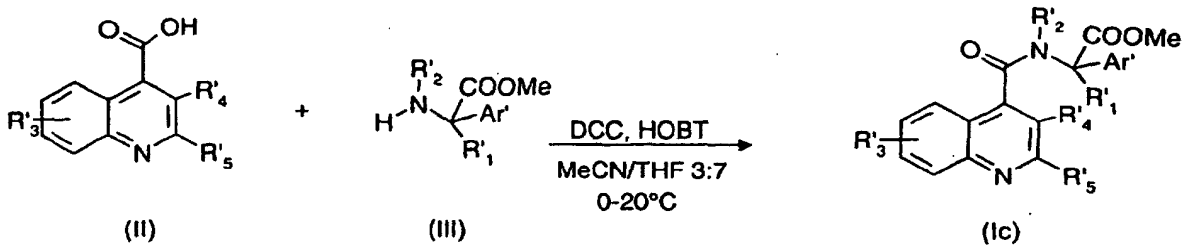
mate; another suitable derivative is an activated ester such as a cyanomethyl ester, thiophenyl ester, p-nitrophenyl ester, p-nitrothiophenyl ester, 2,4,6-trichlorophenyl ester, pentachlorophenyl ester, pentafluorophenyl ester, N-hydroxyphtalimido ester, N-hydroxypiperidine ester, N-hydroxysuccinimide ester, N-hydroxy benzotriazole ester; or the carboxy group may be activated using a carbodiimide or N,N'-carbonyldiimidazole.

[0014] For example, in standard methods well known to those skilled in the art, the compounds of formula (III) may be coupled:

(a) with an acid chloride in the presence of an inorganic or organic base in a suitable aprotic solvent such as dimethylformamide (DMF) at a temperature in a range from -70 to 50°C (preferably in a range from -10 to 20°C),

(b) with the acid in the presence of a suitable condensing agent, such as for example N,N'-carbonyl diimidazole (CDI) or a carbodiimide such as dicyclohexylcarbodiimide (DCC) or N-dimethylaminopropyl-N'-ethylcarbodiimide and N-hydroxybenzotriazole (HOBT) to maximise yields and avoid racemization processes (*Synthesis, 453*, **1972**) in an aprotic solvent such as a mixture of acetonitrile (MeCN) and tetrahydrofuran (THF) in a ratio from 1 : 9 to 7 : 3, respectively, at a temperature in a range from -70 to 50°C (preferably in a range from -10 to 25°C) (see Scheme 1),

Scheme 1



(II) (III) (Ic)

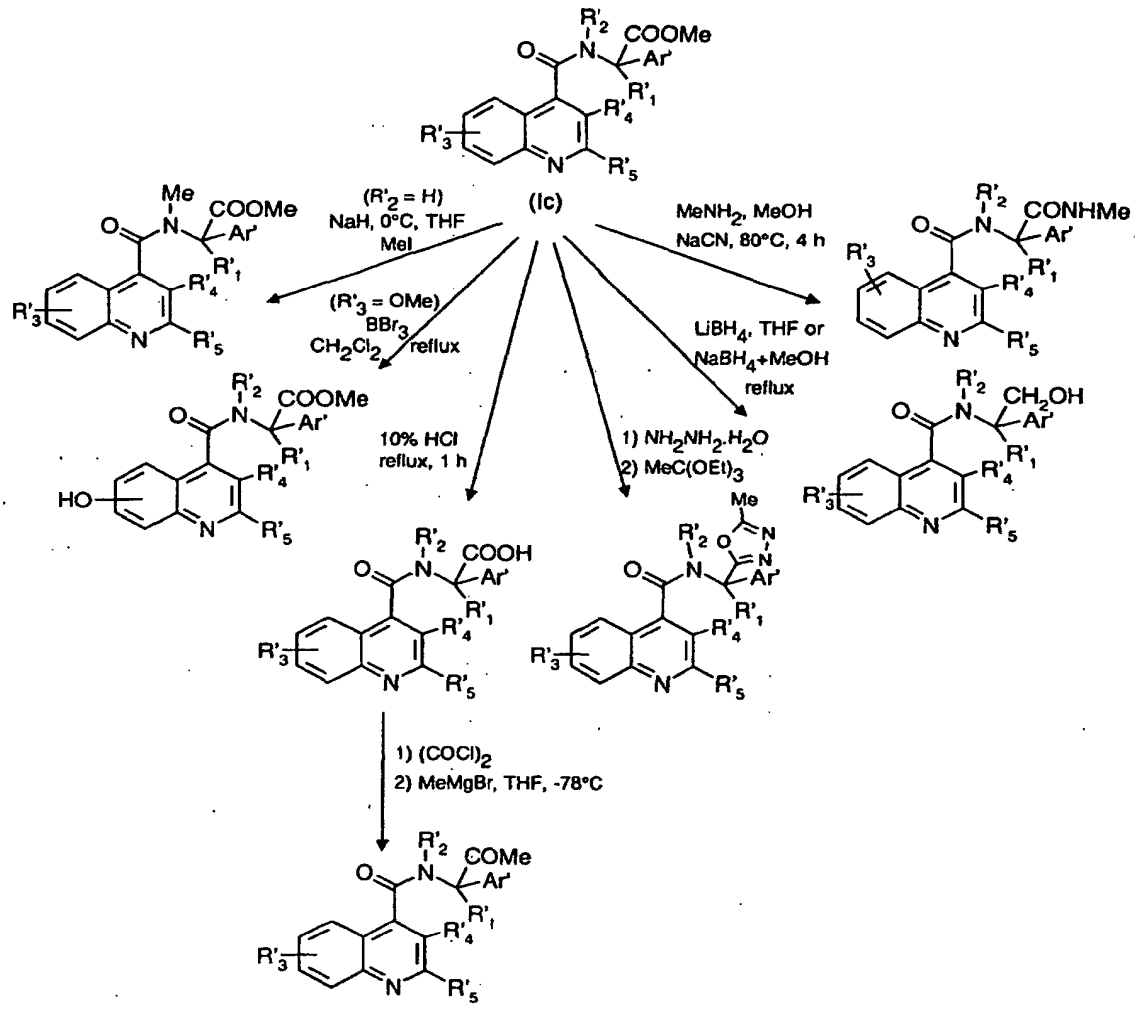
(c) with a mixed anhydride generated in situ from the acid and an alkyl (for example isopropyl) chloroformate in a suitable aprotic solvent such as dichloromethane at a temperature in a range from -70 to 50°C (preferably in a range from -20 to 20°C).

[0015] It will be appreciated that a compound of formula (Ic) may be converted to a compound of formula (I), or one compound of formula (I) may be converted to another compound of formula (I), by interconversion of suitable substituents. Thus, certain compounds of formula (I) and (Ic) are useful intermediates in forming other compounds of the present invention.

For example R'_2 may be hydrogen and converted to R_2 alkyl group, for example methyl, by conventional amide alkylation procedures (Zabicky, *The chemistry of amides*; Interscience, London, 1970, p. 749). When X' is oxygen, it may be converted to X sulphur by standard thioamide formation reagents, such as P_2S_5 (*Chem. Rev., 61*, 45, **1961** or *Angew. Chem.*, 78, 517, **1966**) or the Lawesson reagent (*Tetrahedron*, *41*, 5061, **1985**). When Ar' or R'_5 is a methoxy substituted phenyl, it may be converted to another Ar' or R'_5 hydroxy substituted phenyl by standard demethylation procedures via Lewis acids, such as boron tribromide (*Synthesis*, 249, **1983**) or mineral acids, such as hydrobromic or hydroiodic acid. When R is an alkoxycarbonyl group, for example methoxycarbonyl, it may be converted to another R, such as ethoxycarbonyl by transesterification with an appropriate alcohol at a temperature in a range from 20 to 120°C, carboxy by hydrolysis in acidic or basic medium, aminocarbonyl, alkylaminocarbonyl or dialkylaminocarbonyl by transamidation with ammonia, a primary amine or a secondary amine in methanol as solvent at a temperature in a range from 10 to 120°C, optionally in the presence of a catalytic amount of NaCN (*J. Org. Chem.*, *52*, 2033, **1987**) or by using trimethylaluminium (Me_3Al) (*Tetrahedron Letters*, *48*, 4171, **1977**), hydroxymethyl by a selective metal hydride reduction, such as lithium borohydride reduction (*Tetrahedron, 35*, 567, **1979**) or sodium borohydride reduction in THF + MeOH (*Bull. Chem. Soc. Japan*, *57*, 1948, **1984** or *Synth. Commun.*, *12*, 463, **1982**), alkylcarbonyl by acyl chloride formation and subsequent reaction with alkylmagnesium halides in THF as solvent at a temperature in a range from -78 to 30°C (*Tetrahedron Letters*, 4303, **1979**) or with alkylcadmium halides or dialkylcadmium in the presence of $MgCl_2$ or LiCl (*J. Org. Chem, 47*, 2590, **1982**). Another group which R' as methoxycarbonyl can be converted into is a substituted heteroaromatic ring, such as an oxadiazole (*J. Med. Chem., 34*, 2726, **1991**).

[0016] Scheme 2 summarizes some of the above described procedures to convert a compound of formula (Ic) or (I) in which X' is oxygen, R' is COOMe, Ar' and R'_1 to R'_5 are as described for formula (I) to another compound of formula (I).

Scheme 2

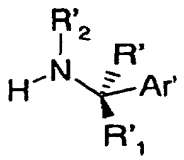


[0017] The compounds of formula (I) may be converted into their pharmaceutically acceptable acid addition salts by reaction with the appropriate organic or mineral acids.

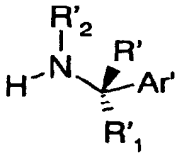
[0018] Solvates of the compounds of formula (I) may be formed by crystallization or recrystallization from the appropriate solvent. For example, hydrates may be formed by crystallization or recrystallization from aqueous solutions, or solutions in organic solvents containing water.

Also salts or solvates of the compounds of formula (I) which are not pharmaceutically acceptable may be useful as intermediates in the production of pharmaceutically acceptable salts or solvates. Accordingly such salts or solvates also form part of this invention.

[0019] As mentioned before, the compounds of formula (I) may exist in more than one stereoisomeric form and the process of the invention may produce racemates as well as enantiomerically pure forms. To obtain pure enantiomers, appropriate enantiomerically pure primary or secondary amines of formula (IIId) or (IIIe)

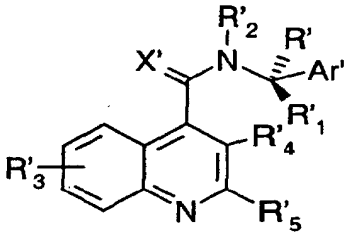


(IIId)

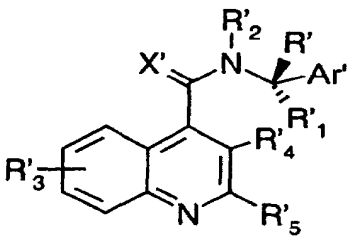


(IIIe)

are reacted with compounds of formula (II), to obtain compounds of formula (I'd) or (I'e).

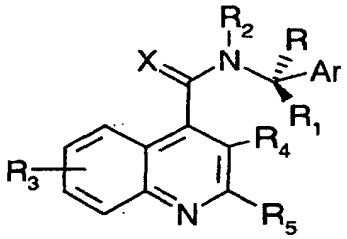


(I'd)

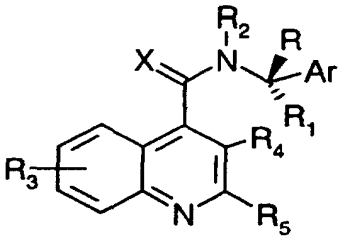


(I'e)

[0020] Compounds of formula (I'd) or (I'e) may subsequently be converted to compounds of formula (Id) or (Ie) by the methods of conversion mentioned before.



(Id)



(Ie)

[0021] Compounds of formula (II) are known compounds or can be prepared from known compounds by known methods.

[0022] For example, the compound of formula (II), in which X' is oxygen, R'_3, R'_4 and R'_5 are hydrogen is described in Pfitzinger, *J. Prakt. Chem.*, *38*, 582, **1882** and in Pfitzinger, *J. Prakt. Chem., 56*, 293, **1897**; the compound of formula (II), in which X' is oxygen, R'_3 and R'_4 are hydrogen and R'_5 is 2-pyridyl is described in Risaliti, *Ric. Scient., 28*, 561, **1958**; the compound of formula (II), in which X' is oxygen, R'_3 and R'_4 are hydrogen and R'_5 is *o*-, *m*- and *p*-chlorophenyl, *o*-fluorophenyl and 3,4-dichlorophenyl are described in Brown *et al.*, *J. Am. Chem. Soc., 68*, 2705, **1946**; the compound of formula (II), in which X' is oxygen, R'_3 and R'_4 are hydrogen and R'_5 is *p*-methoxyphenyl is described in Ciusa and Luzzatto, *Gazz. Chim. Ital., 44*, 64,**1914**; the compound of formula (II), in which X' is oxygen, R'_3 and R'_4 are hydrogen and R'_5 is *m*-trifluoromethylphenyl is described in Shargier and Lalezari, *J. Chem. Eng. Data, 8*, 276, **1963**; the compound of formula (II), in which X' is oxygen, R'_3 and R'_4 are hydrogen and R'_5 is *p*-fluorophenyl is described in Bu Hoi *et al., Rec Trav. Chim., 68*, 781, **1949**; the compound of formula (II), in which X' is oxygen, R'_3 and R'_4 are hydrogen and R'_5 is *p*-methylphenyl is described in Prevost *et al.*, *Compt. Rend. Acad. Sci., 258*, 954, **1964**; the compound of formula (II), in which X' is oxygen, R'_3 and R'_4 are hydrogen and R'_5 is *p*-bromophenyl is described in Nicolai *et al, Eur. J. Med. Chem.*, 27, 977, **1992**; the compound of formula (II) in which X' is oxygen, R'_4 and R'_5 are hydrogen and R'_3 is 6-methyl is described in Buchmann and Howton, *J. Am. Chem. Soc., 68*, 2718, **1946**; the compound of formula (II), in which X' is oxygen, R'_4 and R'_5 are hydrogen and R'_3 is 8-nitro is described in Buchmann *et al, J. Am. Chem. Soc., 69*, 380, **1947**; the compound of formula (II), in which X' is oxygen, R'_4 is hydrogen, R'_3 is 6-chloro, R'_5 is p-chlorophenyl

is described in Lutz *et al., J. Am. Chem. Soc., 68*, 1813, **1946**; the compound of formula (II), in which X' is oxygen, R'_3 and R'_4 are hydrogen and R'_5 is 2-thiazolyl is described in **Eur. Pat. Appl. EP 112,776**; compounds of formula (II), in which X' is oxygen, R'_3 is 8-trifluoromethyl, R'_4 is hydrogen and R'_5 are phenyl, *o*- and *p*-fluorophenyl, 3,4-dichlorophenyl, *p*-methoxyphenyl are described in Nicolai *et al., Eur. J. Med. Chem.*, *27*, 977,**1992**; compounds of formula (II), in which X' is oxygen, R'_3 is 6-bromo, R'_4 is hydrogen and R'_5 are phenyl or *p*-fluorophenyl are described in Nicolai *et al.*, *Eur. J. Med. Chem.*, 27, 977, **1992**; other compounds of formula (II) are described in **Ger. Offen. DE 3,721,222** and in **Eur. Pat. Appl. EP 384,313.**

[0023] Compounds of formula (III), (IIId) and (IIIe) are commercially available compounds or can be prepared from known compounds by known methods (for example, compounds of formula (III) in which R' is alkoxycarbonyl, R'_1 and R'_2 are hydrogen and Ar' is as defined for the compounds of formula (I), are described in *Liebigs Ann. der Chemie, 523*, 199, **1936**).

[0024] The activity of the compounds of formula (I) as NK_3 receptor antagonists in standard tests indicates that they are of potential therapeutic utility in the treatment of both the Primary and Secondary Disorders herein before referred to. The discovery that NK_3 receptor antagonists have potential therapeutic utility in treating the Secondary Disorders is new, and in a further aspect of the present invention there is provided the use of an NK_3 receptor antagonist for the treatment of the Secondary Disorders. There is also provided the use of an NK_3 receptor antagonist in the manufacture of a medicament for the treatment of any of the Secondary Disorders.

The present invention also provides a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, for use as an active therapeutic substance.

[0025] The present invention further provides a pharmaceutical composition comprising a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier.

[0026] The present invention also provides the use of a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for the treatment of the Primary and Secondary Disorders.

[0027] Such a medicament, and a composition of this invention, may be prepared by admixture of a compound of the invention with an appropriate carrier. It may contain a diluent, binder, filler, disintegrant, flavouring agent, colouring agent, lubricant or preservative in conventional manner.

[0028] These conventional excipients may be employed for example as in the preparation of compositions of known agents for treating the conditions.

[0029] Preferably, a pharmaceutical composition of the invention is in unit dosage form and in a form adapted for use in the medical or veterinarial fields. For example, such preparations may be in a pack form accompanied by written or printed instructions for use as an agent in the treatment of the conditions.

[0030] The suitable dosage range for the compounds of the invention depends on the compound to be employed and on the condition of the patient. It will also depend, inter alia, upon the relation of potency to absorbability and the frequency and route of administration.

[0031] The compound or composition of the invention may be formulated for administration by any route, and is preferably in unit dosage form or in a form that a human patient may administer to himself in a single dosage. Advantageously, the composition is suitable for oral, rectal, topical, parenteral, intravenous or intramuscular administration. Preparations may be designed to give slow release of the active ingredient.

[0032] Compositions may, for example, be in the form of tablets, capsules, sachets, vials, powders, granules, lozenges, reconstitutable powders, or liquid preparations, for example solutions or suspensions, or suppositories.

[0033] The compositions, for example those suitable for oral administration, may contain conventional excipients such as binding agents, for example syrup, acacia, gelatin, sorbitol, tragacanth, or polyvinylpyrrolidone; fillers, for example lactose, sugar, maize-starch, calcium phosphate, sorbitol or glycine; tabletting lubricants, for example magnesium stearate; disintegrants, for example starch, polyvinyl-pyrrolidone, sodium starch glycollate or microcrystalline cellulose; or pharmaceutically acceptable setting agents such as sodium lauryl sulphate.

[0034] Solid compositions may be obtained by conventional methods of blending, filling, tabletting or the like. Repeated blending operations may be used to distribute the active agent throughout those compositions employing large quantities of fillers. When the composition is in the form of a tablet, powder, or lozenge, any carrier suitable for formulating solid pharmaceutical compositions may be used, examples being magnesium stearate, starch, glucose, lactose, sucrose, rice flour and chalk. Tablets may be coated according to methods well known in normal pharmaceutical practice, in particular with an enteric coating. The composition may also be in the form of an ingestible capsule, for example of gelatin containing the compound, if desired with a carrier or other excipients.

[0035] Compositions for oral administration as liquids may be in the form of, for example, emulsions, syrups, or elixirs, or may be presented as a dry product for reconstitution with water or other suitable vehicle before use. Such liquid compositions may contain conventional additives such as suspending agents, for example sorbitol, syrup, methyl cellulose, gelatin, hydroxyethylcellulose, carboxymethylcellulose, aluminium stearate gel, hydrogenated edible fats; emulsifying agents, for example lecithin, sorbitan monooleate, or acacia; aqueous or non-aqueous vehicles, which include edible oils, for example almond oil, fractionated coconut oil, oily esters, for example esters of glycerine, or

propylene glycol, or ethyl alcohol, glycerine, water or normal saline; preservatives, for example methyl or propyl p-hydroxybenzoate or sorbic acid; and if desired conventional flavouring or colouring agents.

[0036] The compounds of this invention may also be administered by a non-oral route. In accordance with routine pharmaceutical procedure, the compositions may be formulated, for example for rectal administration as a suppository. They may also be formulated for presentation in an injectable form in an aqueous or non-aqueous solution, suspension or emulsion in a pharmaceutically acceptable liquid, e.g. sterile pyrogen-free water or a parenterally acceptable oil or a mixture of liquids. The liquid may contain bacteriostatic agents, anti-oxidants or other preservatives, buffers or solutes to render the solution isotonic with the blood, thickening agents, suspending agents or other pharmaceutically acceptable additives. Such forms will be presented in unit dose form such as ampoules or disposable injection devices or in multi-dose forms such as a bottle from which the appropriate dose may be withdrawn or a solid form or concentrate which can be used to prepare an injectable formulation.

[0037] The compounds of this invention may also be administered by inhalation, via the nasal or oral routes. Such administration can be carried out with a spray formulation comprising a compound of the invention and a suitable carrier, optionally suspended in, for example, a hydrocarbon propellant.

[0038] Preferred spray formulations comprise micronised compound particles in combination with a surfactant, solvent or a dispersing agent to prevent the sedimentation of suspended particles. Preferably, the compound particle size is from about 2 to 10 microns.

[0039] A further mode of administration of the compounds of the invention comprises transdermal delivery utilising a skin-patch formulation. A preferred formulation comprises a compound of the invention dispersed in a pressure sensitive adhesive which adheres to the skin, thereby permitting the compound to diffuse from the adhesive through the skin for delivery to the patient. For a constant rate of percutaneous absorption, pressure sensitive adhesives known in the art such as natural rubber or silicone can be used.

[0040] As mentioned above, the effective dose of compound depends on the particular compound employed, the condition of the patient and on the frequency and route of administration. A unit dose will generally contain from 20 to 1000 mg and preferably will contain from 30 to 500 mg, in particular 50, 100, 150, 200, 250, 300, 350, 400, 450, or 500 mg. The composition may be administered once or more times a day for example 2, 3 or 4 times daily, and the total daily dose for a 70 kg adult will normally be in the range 100 to 3000 mg. Alternatively the unit dose will contain from 2 to 20 mg of active ingredient and be administered in multiples, if desired, to give the preceding daily dose.

[0041] No unacceptable toxicological effects are expected with compounds of the invention when administered in accordance with the invention.

[0042] The present invention also provides a method for the treatment and/or prophylaxis of the Primary and Secondary Conditions in mammals, particularly humans, which comprises administering to the mammal in need of such treatment and/or prophylaxis an effective amount of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof.

The invention further provides a method for the treatment and/or prophylaxis of the Secondary Conditions in mammals, particularly humans, which comprises administering to the mammal in need of such treatment and/or prophylaxis an effective amount of an NK_3 receptor antagonist.

[0043] The activity of the compounds of the present invention, as NK_3 ligands, is determined by their ability to inhibit the binding of the radiolabelled NK_3 ligands, [^{125}I]-[Me-Phe^7]-NKB or [^{3}H]-Senktide, to guinea-pig and human NK_3 receptors (Renzetti et al, **1991**, *Neuropeptide, 18*, 104-114; Buell et al, **1992**, *FEBS, 299(1)*, 90-95; Chung et al, **1994**, *Biochem. Biophys. Res. Commun.*, *198(3)*, 967-972). The binding assays utilized allow the determination of the concentration of the individual compound required to reduce by 50% the [^{125}I]-[Me-Phe^7]-NKB and [^{3}H]-Senktide specific binding to NK_3 receptor in equilibrium conditions (IC50). Binding assays provide for each compound tested a mean IC_{50} value of 2-5 separate experiments performed in duplicate or triplicate. The most potent compounds of the present invention show IC_{50} values in the range 1-1000 nM; in particular, in guinea-pig cortex membranes by displacement of [^{3}H]-Senktide, the compounds of the Examples 22, 47, 48, and 85 display K_is (nM) of 5.6, 8.8, 12.0 and 4.8 respectively (n=3). The NK_3-antagonist activity of the compounds of the present invention is determined by their ability to inhibit senktide-induced contraction of the guinea-pig ileum (Maggi et al, **1990**, *Br. J. Pharmacol.*, *101*, 996-1000) and rabbit isolated iris sphincter muscle (Hall et al., **1991**, *Eur. J. Pharmacol., 199*, 9-14) and human NK_3 receptors-mediated Ca^{++} mobilization (Mochizuki et al, **1994**, *J. Biol. Chem., 269,* 9651-9658). Guinea-pig and rabbit *in-vitro* functional assays provide for each compound tested a mean K_B value of 3-8 separate experiments, where K_B is the concentration of the individual compound required to produce a 2-fold rightward shift in the concentration-response curve of senktide. Human receptor functional assay allows the determination of the concentration of the individual compound required to reduce by 50% (IC_{50} values) the Ca^{++} mobilization induced by the agonist NKB. In this assay, the compounds of the present invention behave as antagonists. The therapeutic potential of the compounds of the present invention in treating the conditions can be assessed using rodent disease models.

[0044] The following Descriptions illustrate the preparation of the intermediates, whereas the Examples illustrate the preparation of the compounds of the present invention. The compounds of the Examples are summarised in the Tables

1 to 6.

DESCRIPTION 1

2-phenylquinoline-4-carboxylic acid chloride

[0045] 11.7 ml (136.3 mmol) of oxalyl chloride were dissolved in 150 ml of CH_2Cl_2. The solution was cooled at -10°C and 20 g (80.2 mmol) of commercially available 2-phenylquinoline-4-carboxylic acid were added portionwise. The reaction mixture was left overnight at room temperature and then evaporated to dryness to yield 22 g of the title compound, used without further purification.
$C_{16}H_{10}ClNO$
M.W. = 267.76

DESCRIPTION 2

7-methoxy-2-phenylquinoline-4-carboxylic acid

[0046] 5 g (28.2 mmol) of 6-methoxyisatin, 4 ml (33.8 mmol) of acetophenone and 5.2 g (92.6 mmol) of potassium hydroxide were dissolved in 22.9 ml of abs. EtOH and the slurry heated at 80°C for 42 hours. After cooling of the reaction mixture, 50 ml of water were added and the solution extracted with 50 ml of Et_2O. The ice-cooled aqueous phase was acidified to pH 1 with 37% HCl and the precipitate collected by filtration and washed with water.
The solid obtained was dried *in-vacuo* at 40°C to yield 7.0 g of the title compound.
$C_{17}H_{13}NO_3$
M.P. = 226-228°C
M.W. = 279.30

Elemental analysis	Calcd.	C,73.11;	H,4.69;	N,5.01;
	Found	C,72.07;	H,4.59;	N,4.90.

LR. (KBr): 3420; 1630 cm^{-1}.

DESCRIPTION 3

7-methoxy-2-phenylquinoline-4-carboxylic acid chloride

[0047] 2.8 ml (32.3 mmol) of oxalyl chloride were dissolved in 60 ml of CH_2Cl_2. The solution was cooled at -10°C and 6 g (19.0 mmol) of 7-methoxy-2-phenylquinoline-4-carboxylic acid were added portionwise. The reaction mixture was left overnight at room temperature and then evaporated to dryness to yield 7 g of the title compound, used without further purification.
$C_{17}H_{12}ClNO_2$
M.W. = 297.74

DESCRIPTION 4

7-hydroxy-2-phenylquinoline-4-carboxylic acid hydroiodide

[0048] 1.5 g (5.4 mmol) of 7-methoxy-2-phenylquinoline-4-carboxylic acid were added portionwise to 50 ml of 57% aqueous HI. The reaction mixture was refluxed and vigourously stirred for 5 hours; then it was evaporated *in-vacuo* to dryness to yield 2.1 g of the title compound.
$C_{16}H_{11}NO_3$. HI
M.W. = 393.17
I.R. (KBr): 3120; 1650; 1620 cm^{-1}.

DESCRIPTION 5

2-(2-thienyl)quinoline-4-carboxylic acid

[0049] 5 g (34.0 mmol) of isatin, 4.4 ml (40.8 mmol) of 2-acetylthiophene and 6.3 g (112.2 mmol) of potassium hydroxide were dissolved in 40 ml of abs. EtOH and the slurry heated at 80°C for 16 hours. After cooling of the reaction mixture, 50 ml of water were added and the solution extracted with 50 ml of Et_2O. The ice-cooled aqueous phase was acidified to pH 1 with 37% HCl and the precipitate collected by filtration and washed with water.
The crude product obtained was dried *in-vacuo* at 40°C and triturated with EtOAc to yield 4.8 g of the title compound.
$C_{14}H_9NO_2S$
M.P. = 181-183°C
M.W. = 255.29
I.R. (KBr): 1620 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 8.60 (d, 1H); 8.45 (s, 1H); 8.10 (m, 2H); 7.78 (m, 2H); 7.68 (t, 1H); 7.22 (m, 1H).

DESCRIPTION 6

2-(2-furyl)quinoline-4-carboxylic acid

[0050] 5 g (34.0 mmol) of isatin, 4 ml (40.8 mmol) of 2-acetylfuran and 6.3 g (112.2 mmol) of potassium hydroxide were dissolved in 40.9 ml of abs. EtOH and the slurry heated at 80°C for 12 hours. After cooling of the reaction mixture, 50 ml of water were added and the solution extracted with 50 ml of Et_2O. The ice-cooled aqueous phase was acidified to pH 1 with 37% HCl and the precipitate collected by filtration and washed with water. The crude product obtained was dried *in-vacuo* at 40°C to yield 8.5 g of the title compound.
$C_{14}H_9NO_3$
M.W. = 239.23

DESCRIPTION 7

2-(2-furyl)quinoline-4-carboxylic acid chloride

[0051] 5.2 ml (60.4 mmol) of oxalyl chloride were dissolved in 70 ml of CH_2Cl_2. The solution was cooled at -10°C and 8.5 g (35.5 mmol) of 2-(2-furyl)quinoline-4-carboxylic acid were added portionwise. The reaction mixture was left overnight at room temperature and then evaporated to dryness to yield 9.2 g of the title compound, used without further purification.
$C_{14}H_8ClNO_2$
M.W. = 257.78

DESCRIPTION 8

2-(4-pyridyl)quinoline-4-carboxylic acid hydrochloride

[0052] 5 g (34.0 mmol) of isatin, 4.5 ml (40.8 mmol) of 4-acetylpyridine and 6.3 g (112.2 mmol) of potassium hydroxide were dissolved in 40 ml of abs. EtOH and the slurry heated at 80°C for 12 hours. After cooling of the reaction mixture, 50 ml of water were added and the solution extracted with 50 ml of Et_2O. The ice-cooled aqueous phase was acidified to pH 1 with 37% HCl and the precipitate collected by filtration and washed with water.
The aqueous solution was evaporated *in-vacuo* to dryness, the residue triturated with EtOH and filtered off. Evaporation of the solvent afforded 6.0 g of the crude title compound. This product was combined with the previously obtained precipitate and recrystallized from toluene containing traces of MeOH to yield 4.5 g of the title compound.
$C_{15}H_{10}N_2O_2$.HCl
M.P. = 297-301°C
M.W. = 286.72
I.R. (KBr): 1705; 1635; 1610 cm-1.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 8.90 (d, 2H); 8.70 (m, 2H); 8.50 (s, 2H); 8.28 (d, 1H); 7.89 (dt, 2H).

DESCRIPTION 9

2-(4-pyridyl)quinoline-4-carboxylic acid chloride hydrochloride

[0053] 1.3 ml (10.4 mmol) of oxalyl chloride were dissolved in 60 ml of CH_2Cl_2. The solution was cooled at -10°C and 3.0 g (14.4 mmol) of 2-(4-pyridyl)quinoline-4-carboxylic acid hydrochloride were added portionwise. The reaction mixture was left 72 hours at room temperature and then evaporated to dryness to yield 4.0 g of the title compound, used without further purification.
$C_{15}H_9ClN_2O \cdot HCl$
M.W. = 305.22

EXAMPLE 1

(R,S)-N-(α-methylbenzyl)-2-phenylquinoline-4-carboxamide

[0054] 1.2 ml (9.4 mmol) of (R,S) α-methylbenzylamine and 1.6 ml (11.7 mmol) of triethylamine (TEA) were dissolved, under nitrogen athmosphere, in 50 ml of a 1:1 mixture of dry CH_2Cl_2 and CH_3CN.
2.0 g (7.8 mmol) of 2-phenylquinoline-4-carbonylchloride, dissolved in 50 ml of a 1:4 mixture of dry CH_2Cl_2 and DMF, were added dropwise to the ice-cooled solution of the amines and the reaction was kept at 0°- 5°C for 1 hour and left at room temperature overnight.
The reaction mixture was evaporated *in-vacuo* to dryness, the residue was dissolved in EtOAc and washed twice with a sat. sol. of $NaHCO_3$. The organic layer was separated, dried over Na_2SO_4, filtered and evaporated *in-vacuo* to dryness.
The residual oil was crystallized from EtOAc to yield 1.1 g of the title compound as a white solid.
$C_{24}H_{20}N_2O$
M.P. = 156-157°C
M.W. = 352.43

Elemental analysis	Calcd.	C,81.79;	H,5.72;	N,7.95;
	Found	C,81.99;	H,5.69;	N,7.89.

I.R. (KBr): 3240;1645 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 9.29 (d, 1H); 8.32 (d, 2H); 8.13 (d, 1H); 8.13 (s, 1H); 8.06 (d, 1H); 7.81 (ddd, 1H); 7.68-7.52 (m, 4H); 7.47 (d, 2H); 7.39 (dd, 2H); 7.27 (dd, 1H); 5.30 (dq, 1H); 1.52 (d, 3H).

MS (EI; source 200 °C; 70 V; 200 mA): 352 (M+.); 337; 232; 204; 77.

EXAMPLE 2

S-(+)-N-(α-methylbenzyl)-2-phenylquinoline-4-carboxamide

[0055] Prepared as Ex. 1 from 1.2 ml (9.4 mmol) of S-(-)-α-methylbenzylamine, 1.6 ml (11.7 mmol) of TEA, 2.0 g (7.8 mmol) of 2-phenylquinoline-4-carbonylchloride in 100 ml of a mixture of CH_2Cl_2, CH_3CN and DMF.
The work-up of the reaction mixture was carried out in the same manner as described in Ex. 1. The residual oil was crystallized from EtOAc to yield 1.1 g of the title compound.
$C_{24}H_{20}N_2O$
M.P. = 161-162°C
M.W. = 352.43
$[\alpha]_D^{20}$ = + 25 (C = 0.5, DMF)
I.R. (KBr): 3240; 1645 cm^{-1}.

300 MHz ^{1}H-NMR DMSO-d_6): δ 9.29 (d, 1H); 8.32 (d, 2H); 8.13 (d, 1H); 8.13 (s, 1H); 8.06 (d, 1H); 7.81 (ddd, 1H); 7.68-7.52 (m, 4H); 7.47 (d, 2H); 7.39 (dd, 2H); 7.27 (dd, 1H); 5.30 (dq, 1H); 1.52 (d, 3H).

MS spactra was identical to that of the Ex. 1.

EXAMPLE 3

R-(-)-N-(α-methylbenzyl)-2-phenylquinoline-4-carboxamide

[0056] Prepared as Ex. 1 from 1.2 ml (9.4 mmol) of R-(+)-α-methylbenzylamine, 1.6 ml (11.7 mmol) of TEA and 2.0 g (7.8 mmol) of 2-phenylquinoline-4-carbonylchloride in 100 ml of a mixture of CH_2Cl_2, CH_3CN and DMF. The work-up of the reaction mixture was carried out in the same manner as described in Ex. 1. The residual oil was crystallized from EtOAc to yield 1.1 g of the title compound.
$C_{24}H_{20}N_2O$
M.P. = 158-160°C
M.W. = 352.43
$[\alpha]_D^{20}$= - 25 (C = 0.5, DMF)
I.R. (KBr): 3240; 1645 cm^{-1}.
The ^{1}H-NMR and MS spectra were identical to those of the Ex. 1 and Ex. 2.

EXAMPLE 4

(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-phenylquinoline-4-carboxamide

[0057] 2.0 g (8.0 mmol) of 2-phenylquinoline-4-carboxylic acid were dissolved, under nitrogen athmosphere, in 130 ml of dry THF and 100 ml of CH_3CN.
2.0 g (9.9 mmol) of (D,L) methyl phenylglicinate hydrochloride and 1.5 ml (10.7 mmol) of TEA were added and the reaction mixture was cooled at 5°C.
2.5 g (12.1 mmol) of dicyclohexylcarbodiimide (DCC), dissolved in 10 ml of dry CH_2Cl_2, were added dropwise and the solution was allowed to reach room temperature, stirred for 5 hours and left overnight.
The precipitated dicyclohexylurea was filtered off and the solution was evaporated *in-vacuo* to dryness. The residue was dissolved in CH_2Cl_2 and then washed with H_2O. The organic layer was separated, dried over Na_2SO_4 and evaporated *in-vacuo* to dryness to obtain 6.0 g of a crude product which was dissolved in 20 ml of CH_2Cl_2 and left overnight. Some more dicyclohexylurea precipitated and was filtered off. The solution was evaporated *in-vacuo* to dryness and the residue flash chromatographed on 230-400 mesh silica gel, eluting with a mixture of hexane/ethyl acetate 3:2 containing 0.5% NH_4OH. The crude solid obtained was triturated with warm *i*-Pr_2O, filtered, washed and dried to yield 1.1 g of the title compound.
$C_{25}H_{20}N_2O_3$
M.P. = 170-172°C
M. W. = 396.45

Elemental analysis	Calcd.	C,75.74;	H,5.09;	N,7.07;
	Found	C,75.88;	H,5.12;	N,7.06.

I.R. (nujol): 3240; 1750; 1670 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 9.72 (d, 1H); 8.28 (dd, 2H); 8.20 (dd, 1H); 8.13 (dd, 1H); 8.11 (s, 1H); 7.83 (ddd, 1H); 7.66 (ddd, 1H); 7.60-7.50 (m, 5H); 7.47-7.37 (m, 3H); 5.78 (d, 1H); 3.72 (s, 3H).

MS (EI; source 200 °C; 70 V; 200 mA): 396 (M+.); 337; 232; 204.

EXAMPLE 5

(+)-(S)-N-[α-(methoxycarbonyl)benzyl]-2-phenylquinoline-4-carboxamide

[0058] 2.0 g (8.0 mmol) of 2-phenylquinoline-4-carboxylic acid were dissolved, under nitrogen athmosphere, in 70 ml of dry THF and 30 ml of CH_3CN.
1.7 g (8.4 mmol) of (L) methyl phenylglicinate hydrochloride, 1.1 ml (9.9 mmol) of N-methylmorpholine and 2.1 g (15.5 mmol) of N-hydroxybenzotriazole (HOBT) were added and the reaction mixture was cooled at 0°C.
1.85 g (9.0 mmol) of DCC, dissolved in 10 ml of CH_2Cl_2, were added dropwise and the solution was kept at 0°- 5°C

for 1 hour and then at room temperature for 2 hours. The precipitated dicyclohexylurea was filtered off and the solution evaporated *in-vacuo* to dryness. The residue was dissolved in CH_2Cl_2 and washed with H_2O, sat. sol. $NaHCO_3$, 5% citric acid, sat. sol. $NaHCO_3$ and sat. sol. NaCl.
The organic layer was separated, dried over Na_2SO_4 and evaporated *in-vacuo* to dryness; the residue was dissolved in 20 ml of CH_2Cl_2 and left overnight. Some more dicyclohexylurea precipitated and was filtered off.
The solution was evaporated *in-vacuo* to dryness to obtain 2.6 g of a crude product which was triturated with petroleum ether, filtered, washed with *i*-Pr_2O and then recrystallized from 70 ml of *i*-PrOH to yield 1.7 g of the title compound.
$C_{25}H_{20}N_2O_3$
M.P. = 180-181°C
M.W. = 396.45
I.R. (nujol): 3300; 1750; 1640 cm^{-1}.
$[\alpha]_D^{20}$ = +42.0 (C = 0.5, MeOH).
The ^{1}H-NMR and MS spectra were identical to those of Ex. 4.

EXAMPLE 6

(-)-(R)-N-[α-(methoxycarbonyl)benzyl]-2-phenylquinoline-4-carboxamide

[0059] Prepared as Ex. 5 from 2.0 g (8.0 mmol) of 2-phenylquinoline-4-carboxylic acid, 1.7 g (8.4 mmol) of (D) methyl phenylglicinate hydrochloride, 1.1 ml (9.9 mmol) of N-methylmorpholine, 2.1 g (15.5 mmol) of HOBT and 1.85g (9.0 mmol) of DCC in 70 ml of dry THF and 30 ml of CH_3CN.
The work-up of the reaction mixture was carried out in the same manner as described in Ex. 5. The crude product obtained (3.5 g) was triturated twice with warm *i*-Pr_2O, filtered, washed and then recrystallized from 80 ml of *i*-PrOH to yield 2.3 g of the title compound.
$C_{25}H_{20}N_2O_3$
M.P. = 180-181°C
M.W. = 396.45
I.R. (nujol): 3300; 1750; 1640 cm^{-1}.
$[\alpha]_D^{20}$ = -42.0 (C = 0.5, MeOH).
The ^{1}H-NMR and MS spectra were identical to those of Exs. 4 and 5.

EXAMPLE 7

(R,S)-N-[α-(methoxycarbonyl)benzyl]-7-methoxy-2-phenylquinoline-4-carboxamide

[0060] 1.0 g (5.0 mmol) of (D,L) methyl phenylglicinate hydrochloride were dissolved, under nitrogen athmosphere, in 30 ml of dry DMF.
2.5 g (18.1 mmol) of anhydrous potassium carbonate were added and the solution cooled at 0°C.
0.7 g (2.3 mmol) of the compound of Description 3, dissolved in 25 ml of dry DMF, were added dropwise and the solution was kept at 0°- 5°C for 1 hour and at room temperature overnight.
The reaction mixture was evaporated *in-vacuo* to dryness and the residue was dissolved in EtOAc and washed twice with H_2O. The organic layer was separated, dried over Na_2SO_4, filtered and evaporated *in-vacuo* to dryness.
The residual oil was flash chromatographed on 230-400 mesh silica gel, eluting with a mixture of hexane/ethyl acetate 3:2 containing 0.5% NH_4OH to afford 0.1 g of the crude product which was triturated with *i*-Pr_2O to yield 0.08 g of the title compound.
$C_{26}H_{22}N_2O_4$
M.P. = 187-190°C
M.W. = 426.48
I.R. (KBr): 3220; 1750; 1660; 1620 cm^{-1}.

300 MHz ^{1}H-NMR ($CDCl_3$): δ: 8.13-8.08 (m, 3H); 7.80 (s, 1H); 7.55-7.38 (m, 9H); 7.21 (dd, 1H); 7.02 (d broad, H); 5.88 (d, 1H); 3.97 (s,3H); 3.80 (s, 3H).

MS (EI; source 200 °C; 70 V; 200 mA): 426 (M+.); 367 ; 262 ; 234; 191;77.

EXAMPLE 8

(R,S)-N-[α-(methoxycarbonyl)benzyl]-7-hydroxy-2-phenylquinoline-4-carboxamide

[0061] Prepared as Ex. 5 from 2.1 g (5.3 mmol) of the compound of Description 4, 1.08 g (5.3 mmol) of (D,L) methyl phenylglicinate hydrochloride, 1.5 ml (10.7 mmol) of TEA, 1.7 g (12.5 mmol) of HOBT and 1.2 g (5.8 mmol) of DCC in 70 ml of dry THF and 30 ml of CH_3CN.
The work-up of the reaction mixture was carried out in the same manner as described in Ex. 5. The crude product obtained was triturated with *i*-Pr_2O and then recrystallized twice from *i*-PrOH to yield 0.06 g of the title compound.
$C_{25}H_{20}N_2O_4$
M.P. = 256-257°C
M.W. = 412.45
I.R. (KBr): 3270; 1750; 1650; 1620 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 10.30 (s broad, 1H); 9.64 (d, 1H); 8.22 (d, 2H); 8.04 (d, 1H); 7.85 (s, 1H); 7.60-7.34 (m, 9H); 7.21 (dd, 1H); 5.74 (d, 1H); 3.71 (s, 3H).

MS (EI; source 200 °C; 70 V; 200 mA): 412 (M+.); 353; 248; 220; 77.

EXAMPLE 9

(R,S)-N-[α-(carboxy)benzyl]-7-methoxy-2-phenylquinoline-4-carboxamide hydrochloride

[0062] 0.18 g (0.4 mmol) of the product of Ex. 7 were dissolved in 10 ml of 10% HCl and 5 ml of dioxane. The reaction mixture was refluxed and stirred for 3 hours, then evaporated *in-vacuo* to dryness.
The crude product was triturated with warm EtOAc (containing a few drops of EtOH) to yield 0.16 g of the title compound.
$C_{25}H_{20}N_2O_4$.HCl
M.P. = 228-230°C
M.W. = 448.91
I.R. (KBr): 3180; 1735; 1655; 1630 cm^{-1}

300 MHz ^{1}H-NMR (DMSO-d_6): δ 9.6 (d, 1H); 8.26 (dd, 2H); 8.14 (d, 1H); 7.98 (s, 1H); 7.63-7.52 (m, 6H); 7.46-7.36 (m, 3H); 7.33 (dd, 1H); 5.66 (d, 1H); 3.98 (s, 3H).

MS (EI; source 200 °C; 70 V; 200 mA): 412 (M+.); 368 ; 262; 234; 191; 77.

EXAMPLE 10

(R,S)-N-[α-(methylaminocarbonyl)benzyl]-2-phenylquinoline-4-carboxamide

[0063] 0.45 g (1.1 mmol) of the product of Ex. 4 were dissolved in 40 ml of 33% $MeNH_2$/EtOH; a catalitic amount of NaCN was added and the reaction mixture was heated at 70°C for 1 hour in a parr apparatus. The internal pressure rised to 40 psi. The solution was evaporated *in-vacuo* to dryness and the residue was triturated with water, filtered, dried and recrystallized from a mixture of *i*-PrOH (50 ml) and EtOH (30 ml) to yield 0.2 g of the title compound.
$C_{25}H_{21}N_3O_2$
M.P. = 261-263°C
M.W. = 395.47

Elemental analysis	Calcd.	C,75.93;	H.5.35;	N,10.63;
	Found	C,75.65;	H,5.34;	N,10.55.

I.R. (KBr): 3300; 3270; 1660; 1635 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 9.48 (d, 1H); 8.33-8.25 (m, 3H); 8.18-8.10 (m, 3H); 7.80 (ddd, 1H); 7.68-7.50 (m, 6H); 7.40-7.28 (m, 3H); 5.75 (d, 1H); 2.63 (d,3H).

MS (EI; source 200 °C; 70 V; 200 mA): 395 (M+.); 337; 232; 204; 77.

EXAMPLE 11

(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(2-thienyl)quinoline-4-carboxamide

[0064] Prepared as Ex. 5 from 2.0 g (7.3 mmol) of 2-(2-thienyl)quinoline-4-carboxylic acid, 1.7 g (8.4 mmol) of (D,L) methyl phenylglicinate hydrochloride, 1.1 ml (10 mmol) of N-methylmorpholine, 2.1 g (15.5 mmol) of HOBT and 1.85 g (9.0 mmol) of DCC in 70 ml of dry THF, 30 ml of CH_3CN and 10 ml of CH_2Cl_2.
The work-up of the reaction mixture was carried out in the same manner as described in Ex. 5. The crude product obtained was crystallized from EtOAc and then recrystallized from abs. EtOH to yield 0.9 g of the title compound.
$C_{23}H_{18}N_2O_3S$
M.P. = 178-180°C
M.W. = 402.47

Elemental analysis	Calcd.	C,68.64;	H,4.51;	N,6.96;
	Found	C,67.50;	H,4.99;	N,7.43.

I.R. (KBr): 3300; 1745; 1645 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 9.70 (d, 1H); 8.12 (d, 1H); 8.08 (s, 1H); 8.04 (d, 1H); 8.02 (d, 1H); 7.19 (t, 1H); 7.76 (d, 1H); 7.62 (t, 1H); 7.53 (d, 2H); 7.46-7.37 (m, 3H); 7.3 (dd, 1H); 5.68 (d, 1H); 3.68 (s, 3H).

MS (EI; source 200 °C; 70 V; 200 mA): 402 (M+.); 343; 238; 210; 77.

EXAMPLE 12

(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(2-furyl)quinoline-4-carboxamide

[0065] Prepared as Ex. 1 from 7.2 g (35.5 mmol) of (D,L) methyl phenylglicinate hydrochloride, 12.4 ml (88.8 mmol) of TEA and 9.1 g (35.5 mmol) of crude 2-(2-furyl)quinoline-4-carbonylchloride in 350 ml of a mixture of CH_2Cl_2, CH_3CN and DMF. The work-up of the reaction mixture was carried out in the same manner as described in Ex. 1. The crude product obtained was triturated with MeOH to yield 3.3 g of the title compound.
$C_{23}H_{18}N_2O_4$
M.P. = 178-180°C
M.W. = 386.405

Elemental analysis	Calcd.	C,71.49;	H,4.70;	N,7.25;
	Found	C,71.67;	H,4.74;	N,7.17.

I.R. (KBr): 3300; 1750; 1650 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 9.72 (d, 1H); 8,12 (d, 1H); 8.06 (d, 1H); 7.96 (dd, 1H); 7.92 (s, 1H); 7.80 (ddd, 1H); 7.62 (ddd, 1H); 7.52 (dd, 2H); 7.45-7.35 (m, 4H); 6.73 (dd, 1H); 5.77 (d, 1H); 3.74 (s, 3H).

MS (EI; source 200 °C; 70 V; 200 mA): 386 (M+.); 327; 222; 194; 77.

EXAMPLE 13

(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(4-pyridyl)quinoline-4-carboxamide

[0066] Prepared as Ex. 1 from 3.4 g (16.7 mmol) of (D,L) methyl phenylglicinate hydrochloride, 3.9 ml (27.8 mmol) of TEA and 3.0 g (11.1 mmol) of 2-(4-pyridyl)quinoline-4-carbonylchloride in 100 ml of a mixture of CH_2Cl_2, CH_3CN and DMF. The work-up of the reaction mixture was carried out in the same manner as described in Ex. 1. The crude product obtained was recrystallized three times from EtOAc to yield 1.9 g of the title compound.
$C_{24}H_{19}N_3O_3$

M.P. = 172-174°C
M.W. = 397.43

Elemental analysis	Calcd.	C,72.53;	H,4.82;	N,10.57;
	Found	C,71.87;	H,4.87;	N,10.44.

I.R. (KBr): 3240; 1750; 1670 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 9.74 (d, 1H); 8.79 (dd, 2H); 8.27-8.17 (m, 5H); 7.89 (ddd, 1H); 7.74 (ddd, 1H); 7.54 (dd, 2H); 7.47-7.38 (m, 3H); 5.8 (d, 1H); 3.75 (s, 3H).

MS (EI; source 200 °C; 70 V; 200 mA): 397 (M+.); 338; 233; 205; 77.

EXAMPLE 14

(R,S)-N-[α-(methoxycarbonyl)-2-thienylmethyl]-2-phenylquinoline-4-carboxamide

[0067] Prepared as Ex. 1 from 1.94 g (9.4 mmol) of (D,L) methyl thienylglicinate hydrochloride, 2.7 ml (19.5 mmol) of TEA and 2.0 g (7.8 mmol) of 2-phenylquinoline-4-carbonylchloride in 100 ml of a mixture of CH_2Cl_2, CH_3CN and DMF. The work-up of the reaction mixture was carried out in the same manner as described in Ex. 1. The crude product obtained was recrystallized three times from EtOAc to yield 0.66 g of the title compound.
$C_{23}H_{18}N_2O_3S$
M.P. = 144-145°C
M.W. = 402.47

Elemental analysis	Calcd.	C,68.64;	H,4.51;	N,6.96;
	Found	C,68.81;	H,4.46;	N,6.96.

I.R. (KBr): 3295; 1745; 1640 cm^{-1}.

300 MHz ^{1}H-NMR ($CDCl_3$): δ 8.25 (dd, 1H); 8.22 (dd, 1H); 8.17 (dd, 2H); 7.95 (s, 1H); 7.78 (ddd, 1H); 7.60 (ddd, 1H); 7.56-7.45 (m, 3H); 7.35 (dd,1H) ; 7.20 (d, 1H); 7.05 (dd, 1H); 7.05 (s broad, 1H); 6.22 (d, 1H); 3.9 (s, 3H).

MS (EI; source 200 °C; 70 V; 200 mA): 402 (M+.); 343; 232; 204.

EXAMPLE 15

(R,S)-N-[α-(methoxycarbonylmethyl)benzyl]-2-phenylquinoline-4-carboxamide

[0068] Prepared as Ex. 5 from 1.39 g (5.60 mmol) of 2-phenylquinoline-4-carboxylic acid, 1.2 g (5.60 mmol) of (R, S) methyl 3-amino-3-phenylpropionate hydrochloride, 0.78 ml (5.60 mmol) of TEA, 1.51 g (11.2 mmol) of HOBT and 2.31 g (11.2 mmol) of DCC in 10 ml of dry THF, 4 ml of CH_3CN and 7 ml of CH_2Cl_2. The work-up of the reaction mixture was carried out in the same manner as described in Ex. 5. The crude product obtained was dissolved in CH_2Cl_2 and left at 0°C overnight. Some more dicyclohexylurea precipitated and was filtered off.
The solution was evaporated *in-vacuo* to dryness to obtain 1.4 g of a crude product which was triturated with a mixture of *i*-Pr_2O/acetone 99:1 to yield 1.2 g of the title compound as a white solid.
$C_{26}H_{22}N_2O_3$
M.P. = 156-158°C
M.W. = 410.47

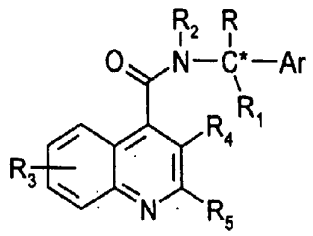
Elemental analysis	Calcd.	C,76.07;	H,5.40;	N,6.82;
	Found	C,75.77;	H,5.38;	N,6.94.

I.R. (KBr): 3295; 1755; 1645; 1590; 1530 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 9.40 (d, 1H); 8.29 (dd, 2H); 8.14 (d, 1H); 8.07 (d, 1H); 8.04 (s, 1H); 7.83 (ddd, 1H); 7.66-7.52 (m, 4H); 7.50 (d, 2H); 7.40 (dd, 2H); 7.31 (ddd, 1H); 5.60 (dt, 1H); 3.65 (s, 3H); 3.04-2.89 (m, 2H).

MS (EI; source 200 °C; 70 V; 200 mA): 410 (M+.); 337; 233; 205.

TABLE 1



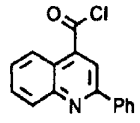
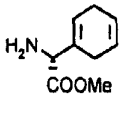
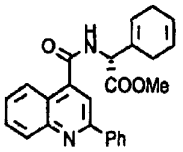
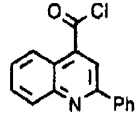
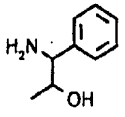
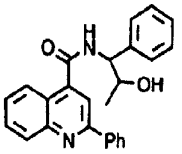
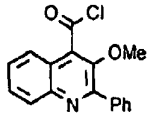
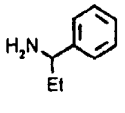
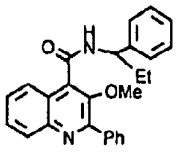
Ex.	Ar	R	R_1	R_2	R_3	R_4	R_5	*	Molecular formula	Melting point °C	$[\alpha]_D^{20}$ c=0.5,MeOH
1	Ph	Me	H	H	H	H	Ph	(R,S)	$C_{24}H_{20}N_2O$	156-157	
2	Ph	Me	H	H	H	H	Ph	(S)	$C_{24}H_{20}N_2O$	161-162	+25° [a]
3	Ph	Me	H	H	H	H	Ph	(R)	$C_{24}H_{20}N_2O$	158-160	-25° [a]
4	Ph	COOMe	H	H	H	H	Ph	(R,S)	$C_{25}H_{20}N_2O_3$	170-172	
5	Ph	COOMe	H	H	H	H	Ph	(S)	$C_{25}H_{20}N_2O_3$	180-181	+42°
6	Ph	COOMe	H	H	H	H	Ph	(R)	$C_{25}H_{20}N_2O_3$	180-181	-42°
7	Ph	COOMe	H	H	7-OMe	H	Ph	(R,S)	$C_{26}H_{22}N_2O_4$	187-190	
8	Ph	COOMe	H	H	7-OH	H	Ph	(R,S)	$C_{25}H_{20}N_2O_4$	256-257	
9	Ph	COOH	H	H	7-OMe	H	Ph	(R,S)	$C_{25}H_{20}N_2O_4$.HCl	228-230	
10	Ph	CONHMe	H	H	H	H	Ph	(R,S)	$C_{25}H_{21}N_3O_2$	261-263	
11	Ph	COOMe	H	H	H	H	2-thienyl	(R,S)	$C_{23}H_{18}N_2O_3S$	178-180	
12	Ph	COOMe	H	H	H	H	2-furyl	(R,S)	$C_{23}H_{18}N_2O_4$	178-180	
13	Ph	COOMe	H	H	H	H	4-Py	(R,S)	$C_{24}H_{19}N_3O_3$	172-174	
14	2-thienyl	COOMe	H	H	H	H	Ph	(R,S)	$C_{23}H_{18}N_2O_3S$	144-145	
15	Ph	CH_2COOMe	H	H	H	H	Ph	(R,S)	$C_{26}H_{22}N_2O_3$	156-158	

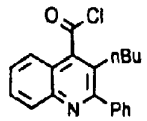
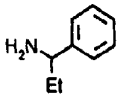
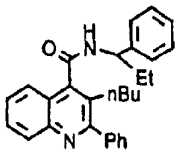
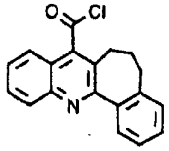
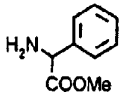
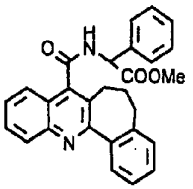
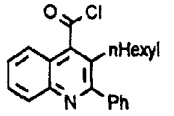
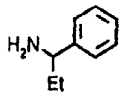
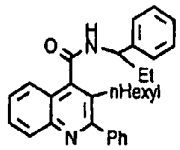
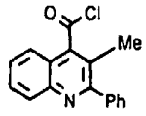
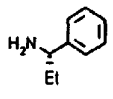
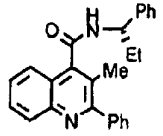
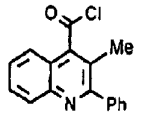
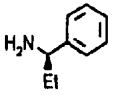
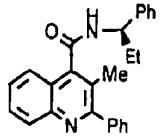
[a] solvent DMF

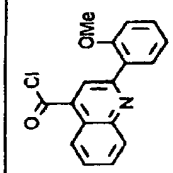
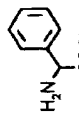
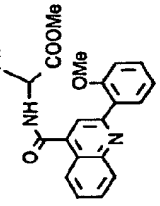
The compounds of the Examples 16-49 of general formula (I) (grouped in the following Table 2) were synthesized starting from the appropriate acyl chlorides of (II) and amines of formula (III) shown in the table and following the synthetic procedure described in Example 1. Acyl chlorides were synthesized starting from the corresponding acid of formula (II) and following Description 1. Reaction yields are calculated on the purified, but unrecrystallized material. Analytical and spectroscopic data of the compounds of the Examples 16-49 are grouped in Table 5.

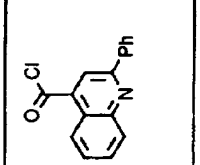
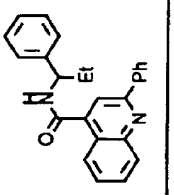
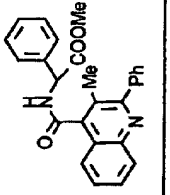
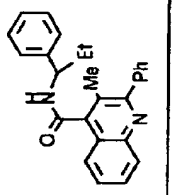
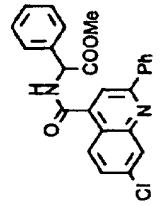
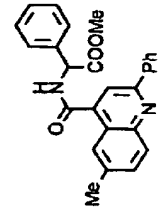
Table 2

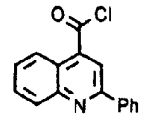
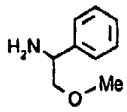
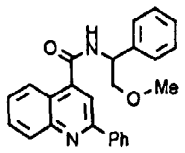
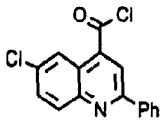
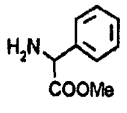
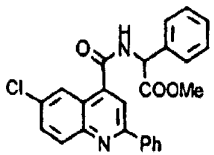
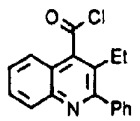
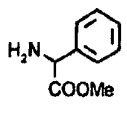
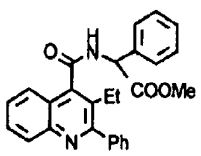
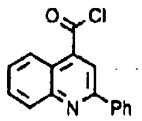
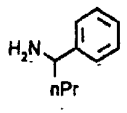
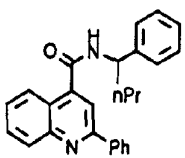
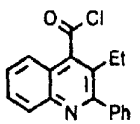
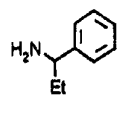
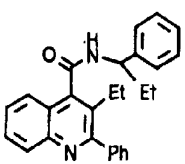
Acyl chloride of (II) + (III) ⟶ (I)

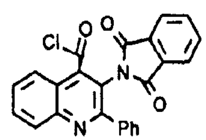
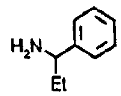
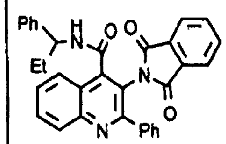
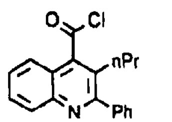
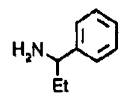
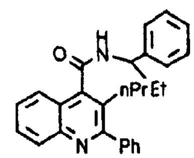
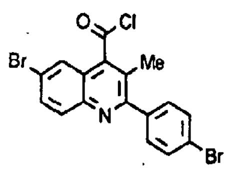
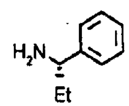
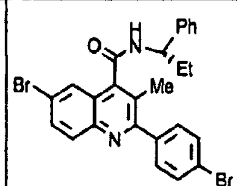
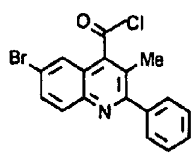
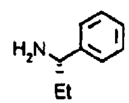
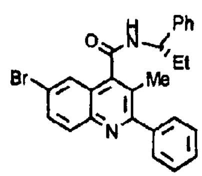
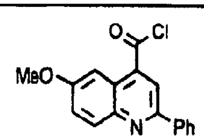
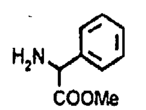
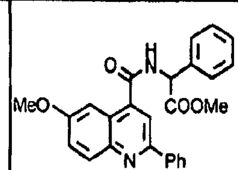
Ex.	Acyl chloride of (II)	(III)	(I)	Stereo chemistry	Molecular formula	M.W.	yield (%)	m.p. (°C) (recryst. solv.)	$[\alpha]_D^{20}$ (c=1, MeOH)
16				(R)	$C_{25}H_{22}N_2O_3$	398.47	16	120-122 (iPr_2O)	- 18.9 (c=0.5)
17				(R,S) single diast.	$C_{25}H_{22}N_2O_2$	382.47	44	204-205 (iPrOH/ iPr_2O)	
18				(R,S)	$C_{26}H_{24}N_2O_2$	396.49	48	163-165 (iPrOH/ iPr_2O)	

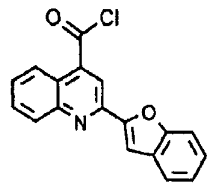
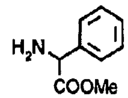
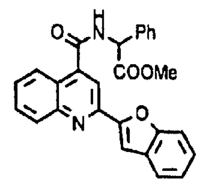
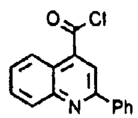
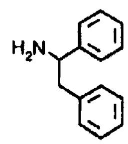
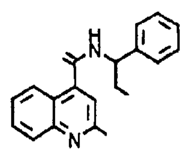
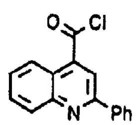
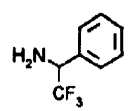
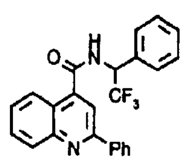
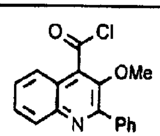
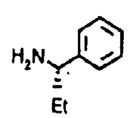
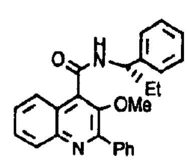
Ex.	Acyl chloride of (II)	(III)	(I)	Stereo chemistry	Molecular formula	M.W.	yield (%)	m.p. (°C) (recryst. solv.)	$[\alpha]_D^{20}$ (c=1, MeOH)
19				(R,S)	$C_{29}H_{30}N_2O$	422.58	30	147-150 (hexane)	
20				(R,S)	$C_{28}H_{24}N_2O_3$	436.52	43	186-188 (iPrOH/ iPr_2O)	
21				(R,S)	$C_{31}H_{34}N_2O$	450.63	24	131-134 (hexane/ iPr_2O)	
22				(S)	$C_{26}H_{24}N_2O$	380.49	58	153-155 (iPr_2O)	- 36.0
23				(R)	$C_{26}H_{24}N_2O$	380.49	78	155-156 (iPr_2O)	+ 35.9

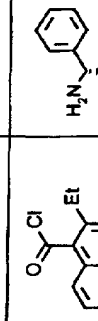
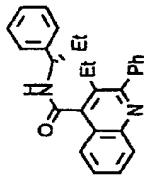
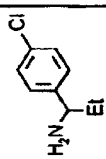
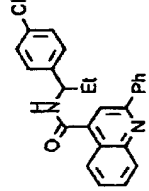
Ex.	Acyl chloride of (II)	(III)	(I)	Stereo chemistry	Molecular formula	M.W.	yield (%)	m.p. (°C) (recryst. solv.)	$[\alpha]_D^{20}$ (c=1, MeOH)
24				(R,S)	$C_{26}H_{22}N_2O_4$	426.48	55	124-125 (toluene)	
25				(R,S)	$C_{31}H_{26}N_2O$	442.57	49	198-200 (toluene)	
26				(R,S)	$C_{25}H_{19}FN_2O_3$	414.44	75	146-147 (toluene)	
27				(R,S)	$C_{25}H_{20}Cl_2N_2O$	435.36	44	193-194 (toluene)	
28				(R,S)	$C_{24}H_{20}N_2O_2$	368.43	24	117-119 (toluene)	

Ex.	Acyl chloride of (II)	(III)	(I)	Stereo chemistry	Molecular formula	M.W.	yield (%)	m.p. (°C) (recryst. solv.)	$[\alpha]_D^{20}$ (c=1, MeOH)
29				(R,S)	$C_{25}H_{22}N_2O$	366.47	80	141-143 (toluene)	
30				(R,S)	$C_{26}H_{22}N_2O_3$	410.48	60	180-181 (toluene / iPr_2O)	
31				(R,S)	$C_{26}H_{24}N_2O$	380.49	55	156-158 (toluene/ hexane)	
32				(R,S)	$C_{25}H_{19}ClN_2O_3$	430.90	48	180-183 (toluene)	
33				(R,S)	$C_{26}H_{22}N_2O_3$	410.48	48	179-181 (toluene)	

Ex.	Acyl chloride of (II)	(III)	(I)	Stereo chemistry	Molecular formula	M.W.	yield (%)	m.p. (°C) (recryst. solv.)	$[\alpha]_D^{20}$ (c=1, MeOH)
34				(R,S)	$C_{25}H_{22}N_2O_2$	382.47	42	144-145 (toluene)	
35				(R,S)	$C_{25}H_{19}ClN_2O_3$	430.90	46	197-199 (toluene)	
36				(R,S)	$C_{27}H_{24}N_2O_3$	424.50	52	156-157 (toluene/ hexane)	
37				(R,S)	$C_{26}H_{24}N_2O$	380.49	50	149-150 (toluene)	
38				(R,S)	$C_{27}H_{26}N_2O$	394.52	53	158-159 (Et_2O/ iPr_2O)	

Ex.	Acyl chloride of (II)	(III)	(I)	Stereo chemistry	Molecular formula	M.W.	yield (%)	m.p. (°C) (recryst. solv.)	$[\alpha]_D^{20}$ (c=1, MeOH)
39				(R,S)	$C_{33}H_{25}N_3O_3$	511.58	16	201-202 (toluene)	
40				(R,S)	$C_{28}H_{28}N_2O$	408.55	71	149-151 (toluene/ hexane)	
41				(S)	$C_{26}H_{22}Br_2N_2O$	538.30	24	230-231 (Et_2O / iPr_2O)	- 49.8 (c=0.2)
42				(S)	$C_{26}H_{23}BrN_2O$	459.40	39	179-180 (hexane/ iPrOH)	-.60.5
43				(R,S)	$C_{26}H_{22}N_2O_4$	426.48	45	209-211 (Me_2CO)	

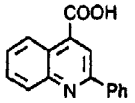
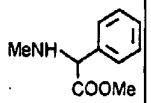
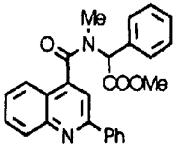
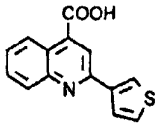
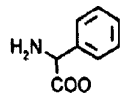
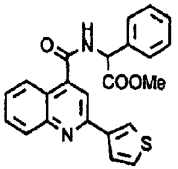
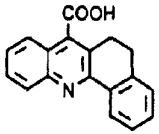
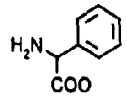
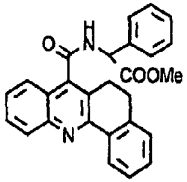
Ex.	Acyl chloride of (II)	(III)	(I)	Stereo chemistry	Molecular formula	M.W.	yield (%)	m.p. (°C) (recryst. solv.)	$[\alpha]_D^{20}$ (c=1, MeOH)
44				(R,S)	$C_{27}H_{20}N_2O_4$	436.47	65	240-241 (EtOAc)	
45				(R,S)	$C_{30}H_{24}N_2O$	428.53	47	194-196 (EtOAc)	
46				(R,S)	$C_{24}H_{17}F_3N_2O$	406.41	45	180-181 (toluene)	
47				(S)	$C_{26}H_{24}N_2O_2$	396.49	58	132-134 (Me_2CO)	- 45 (c=0.5)

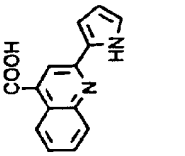
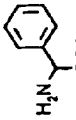
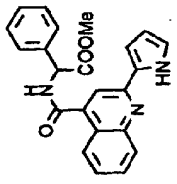
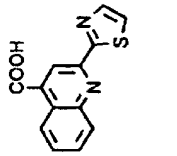
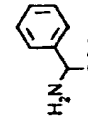
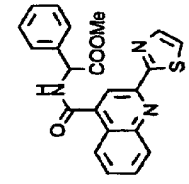
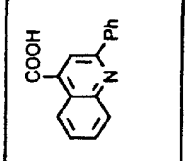
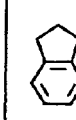
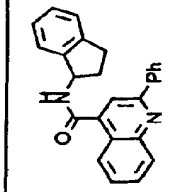
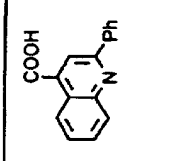
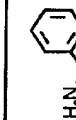
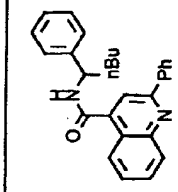
Ex.	Acyl chloride of (II)	(III)	(I)	Stereo chemistry	Molecular formula	M.W.	yield (%)	m.p. (°C) (recryst. solv.)	$[\alpha]D^{20}$ (c=1, MeOH)
48				(S)	$C_{27}H_{26}N_2O$	394.52	53	118-120 (hexane)	- 42 (c=0.5)
49				(R,S)	$C_{25}H_{21}ClN_2O$	400.91	40	177-178 (toluene)	

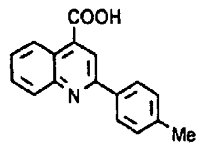
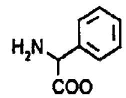
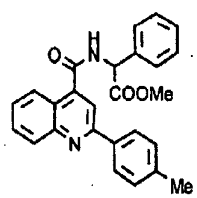
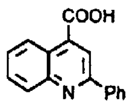
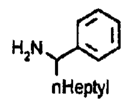
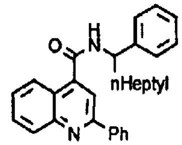
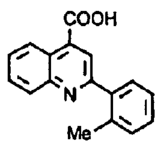
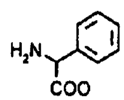
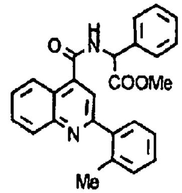
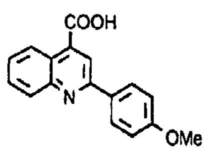
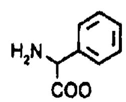
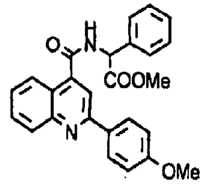
The compounds of the Examples 50-87 of general formula (I) (grouped in the following Table 3) were synthesized starting from the appropriate reagents (II) and (III) shown in the table and following the synthetic procedure described in Example 5. Reaction yields are calculated on the purified, but unrecrystallized material. Analytical and spectroscopic data of the compounds of the Examples 50-87 are grouped in Table 5.

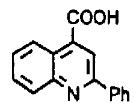
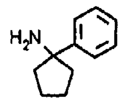
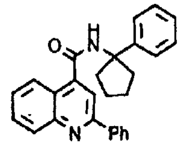
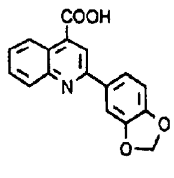
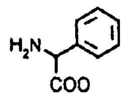
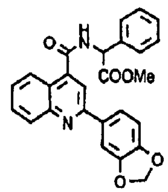
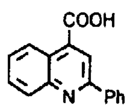
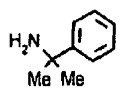
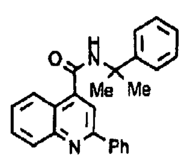
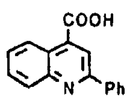
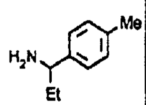
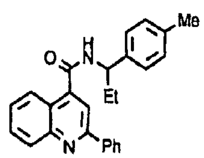
Table 3

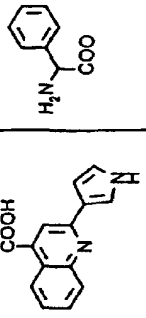
(II) + (III) ⟶ (I)

Ex.	(II)	(III)	(I)	Stereo chemistry	Molecular formula	M.W.	yield (%)	m.p. (°C) (recryst. solv.)	$[\alpha]_D^{20}$ (c=1, MeOH)
50				(R,S)	$C_{26}H_{22}N_2O_3$	410.48	46	128-129 (iPrOH)	
51				(R,S)	$C_{23}H_{18}N_2O_3S$	402.47	88	169-171 (iPrOH)	
52				(R,S)	$C_{27}H_{22}N_2O_3$	422.49	41	217-219 (EtOH abs.)	

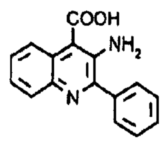
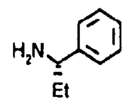
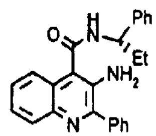
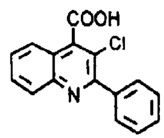
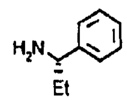
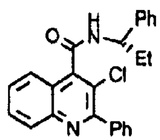
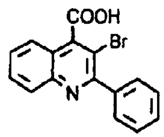
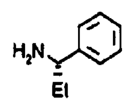
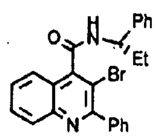
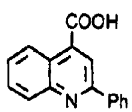
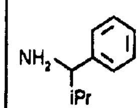
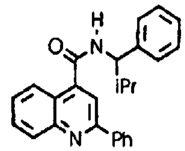
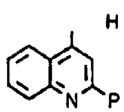
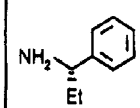
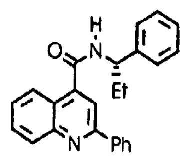
Ex.	(II)	(III)	(I)	Stereo chemistry	Molecular formula	M.W.	yield (%)	m.p. (°C) (recryst. solv.)	$[\alpha]_D^{20}$ (c=1, MeOH)
53				(R,S)	$C_{23}H_{19}N_3O_3$	385.42	44	181-182 (iPrOH)	
54				(R,S)	$C_{22}H_{17}N_3O_3S$	403.45	50	209-211 (iPrOH)	
55				(R,S)	$C_{25}H_{20}N_2O$	364.45	95	183-184 (iPrOH)	
56				(R,S)	$C_{27}H_{26}N_2O$	394.52	77	155-156 (iPrOH/ iPr_2O)	

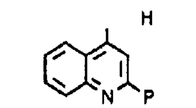
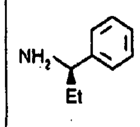
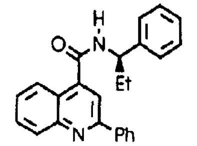
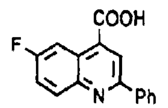
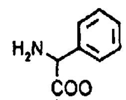
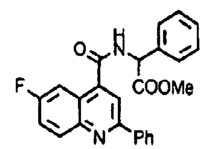
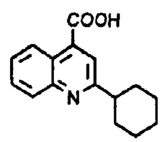
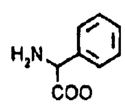
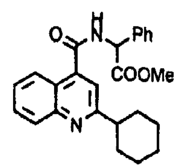
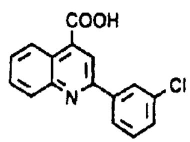
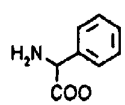
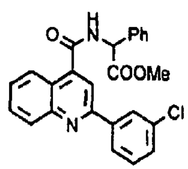
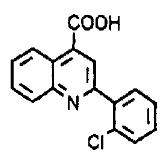
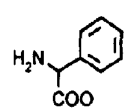
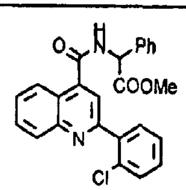
Ex.	(II)	(III)	(I)	Stereo chemistry	Molecular formula	M.W.	yield (%)	m.p. (°C) (recryst. solv.)	$[\alpha]_D^{20}$ (c=1, MeOH)
57				(R,S)	$C_{26}H_{22}N_2O_3$	410.48	83	172-174 (iPrOH)	
58				(R,S)	$C_{30}H_{32}N_2O$	436.60	91	121-128 (iPr_2O)	
59				(R,S)	$C_{26}H_{22}N_2O_3$	410.48	79	180-182 (iPrOH)	
60				(R,S)	$C_{26}H_{22}N_2O_4$	426.48	62	182-183 (iPrOH)	

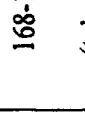
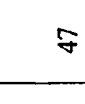
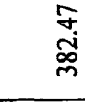
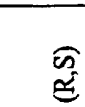
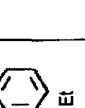
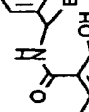
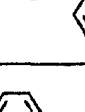
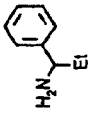
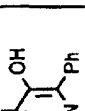
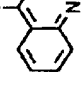
Ex.	(II)	(III)	(I)	Stereo chemistry	Molecular formula	M.W.	yield (%)	m.p. (°C) (recryst. solv.)	$[\alpha]_D^{20}$ (c=1, MeOH)
61				--	$C_{27}H_{24}N_2O$	392.51	82	164-165 (iPrOH)	
63				(R,S)	$C_{26}H_{20}N_2O_5$	440.46	70	186-187 (iPrOH)	
64				--	$C_{25}H_{22}N_2O$	366.47	75	173-174 (iPrOH)	
Ex.	(II)	(III)	(I)	Stereo chemistry	Molecular formula	M.W.	yield (%)	m.p. (°C) (recryst. solv.)	$[\alpha]_D^{20}$ (c=1, MeOH)
65				(R,S)	$C_{26}H_{24}N_2O$	380.49	90	160-162 (iPrOH)	

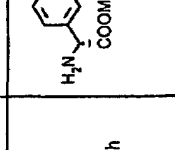
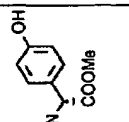
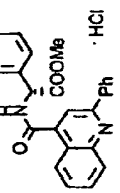
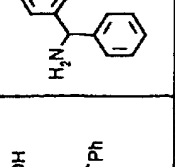
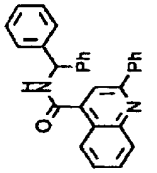
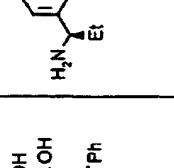
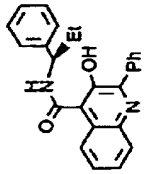
66				(R,S)	$C_{23}H_{19}N_3O_3$	385.42	10	202-204 (iPr_2O)
67				(R,S)	$C_{25}H_{18}Cl_2N_2O_3$	465.34	59	164-165 (iPrOH)
68			(a)	(R)	$C_{24}H_{21}N_3O$	367.45	49	139-141 (iPrOH/ iPr_2O) - 6.9 (c=0.5)

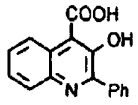
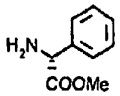
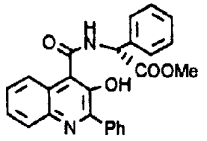
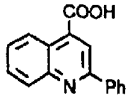
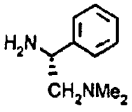
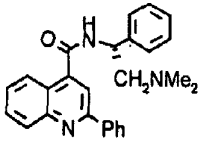
(a) the phthalimido protecting group was removed by refluxing for 4h with hydrate hydrazine in 95% EtOH/1,2 dichloroethane, 9:1 respectively and then adding 37% HCl (up to pH=1) and refluxing an additional hour.

Ex.	(II)	(III)	(I)	Stereo chemistry	Molecular formula	M.W.	yield (%)	m.p. (°C) (recryst. solv.)	$[\alpha]_D^{20}$ (c=1, MeOH)
69				(S)	$C_{25}H_{23}N_3O$	381.48	78	153-155 (iPrOH/ iPr_2O)	- 68.0 (c=0.5)
70				(S)	$C_{25}H_{21}ClN_2O$	400.91	58	137-139 (toluene/ hexane)	- 40.5 (c=0.5)
71				(S)	$C_{25}H_{21}BrN_2O$	445.37	20	119-122 (toluene/ hexane)	- 41.4 (c=0.5)
72				(R,S)	$C_{26}H_{24}N_2O$	380.49	59	165-166 (iPrOH)	
73				(S)	$C_{25}H_{22}N_2O$	366.46	77	140-141 (iPrOH)	- 26.7

Ex.	(II)	(III)	(I)	Stereo chemistry	Molecular formula	M.W.	yield (%)	m.p. (°C) (recryst. solv.)	$[\alpha]_D^{20}$ (c=1, MeOH)
74				(R)	$C_{25}H_{22}N_2O$	366.46	51	151-152 (iPrOH)	+ 26.6
75				(R,S)	$C_{25}H_{19}FN_2O_3$	414.44	44	174-176 (toluene/ EtOAc)	
76				(R,S)	$C_{25}H_{26}N_2O_3$	402.50	53	151-153 (EtOAc)	
77				(R,S)	$C_{25}H_{19}ClN_2O_3$	430.90	68	161-163 (toluene/ hexane)	
78				(R,S)	$C_{25}H_{19}ClN_2O_3$	430.90	43	175-178 (toluene/ hexane)	

Ex.	(II)	(III)	(I)	Stereo chemistry	Molecular formula	M.W.	yield (%)	m.p. (°C) (recryst. solv.)	$[\alpha]_D^{20}$ (c=1, MeOH)
79				(R,S)	$C_{25}H_{22}N_2O_2$	382.47	47	168-169 (toluene)	
80				(R,S)	$C_{27}H_{22}N_2O_5$	454.49	16	193-194 (toluene)	
81				(R,S)	$C_{25}H_{20}N_2O_4$	412.40	32	178-180 (toluene)	
82				(R,S)	$C_{25}H_{18}Cl_2N_2O_3$	465.34	61	142-143 (iPrOH)	

Ex.	(II)	(III)	(I)	Stereo chemistry	Molecular formula	M.W.	yield (%)	m.p. (°C) (recryst. solv.)	$[\alpha]_D^{20}$ (c=1, MeOH)
83				(R)	$C_{25}H_{20}N_2O_4 \cdot HCl$	448.88	50	140 dec. (Me_2CO)	- 7
84				--	$C_{29}H_{22}N_2O$	414.51	42	182-184 (EtOAc)	
85				(R)	$C_{25}H_{22}N_2O_2$	382.47	66	122-125 (hexane/ EtOAc)	+ 27.2 (c=0.5)

Ex.	(II)	(III)	(I)	Stereo chemistry	Molecular formula	M.W.	yield (%)	m.p. (°C) (recryst. solv.)	$[\alpha]_D^{20}$ (c=1, MeOH)
86				(R)	$C_{25}H_{20}N_2O_4$	412.45	70	125-127 (iPr_2O)	- 50 (c=0.5)
87				(R)	$C_{26}H_{25}N_3O$	395.51	26	133-135 (iPr_2O/ iPrOH)	- 11.2 (c=0.5)

The compounds of the Examples 88-91 of general formula (I) (grouped in the following Table 4) were synthesized starting from other compounds of formula (I) (i.e. compounds of formula Ic) and following the synthetic procedures described in Example 10 (for compounds of the Examples 88, 89 and 90) and in Example 9 (for compound of the Example 92). Reaction yields are calculated on the purified, but unrecrystallized material. Analytical and spectroscopic data of the compounds of the Examples 88-91 are grouped in Table 5.

Table 4

(Ic) ⟶ (I)

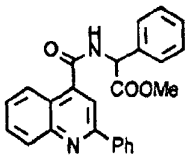
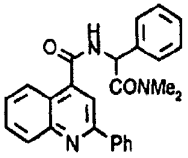
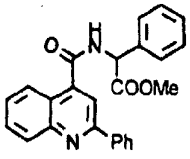
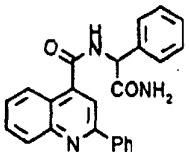
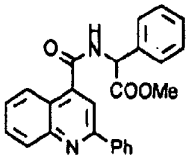
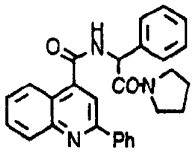
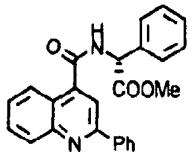
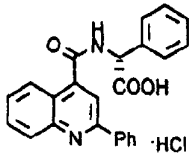
Ex.	(Ic)	(I)	Stereo chemistry	Molecular formula	M.W.	yield (%)	m.p. (°C) (recryst. solv.)	$[\alpha]_D^{20}$ (c=1, MeOH)
88			(R,S)	$C_{26}H_{23}N_3O_2$	409.49	22	219-221 (iPrOH /EtOH)	
89			(R,S)	$C_{24}H_{19}N_3O_2$	381.43	95	237-238 (iPrOH /EtOH)	
90			(R,S)	$C_{28}H_{25}N_3O_2$	435.53	69	199-200 (iPrOH)	
91			(R)	$C_{24}H_{18}N_2O_3$ ·HCl	418.88	94	203-205 (acetone)	- 40.0 (c=0.5)

Table 5. Analytical and spectroscopic data of compounds of Examples **16-91**

Ex.	Elemental analysis	IR (KBr); cm^{-1}	MS (EI; source 200°C; 70 eV; 200 μA)	300 MHz ^1H NMR (DMSO), 303 K
16		3240; 1750; 1640; 1595; 1545	398 (M+.); 232; 204	9.40 (d,1H); 8.30 (d,2H); 8.18 (d,1H); 8.13 (d,1H); 8.10 (s,1H); 7.83 (dd,1H); 7.66 (dd,1H); 7.63-7.51 (m,3H); 5.87 (s br,1H); 5.70 (m,2H); 5.12 (d,1H); 3.80 (s,3H); 2.92-2.60 (m,4H).
17	Calcd. C,78.51; H,5.80; N,7.32 Found C,78.27; H,5.83; N,7.24	3400; 3200; 1640; 1595; 1532	337 (M-C_2H_4OH)+; 232; 204	9.20 (d,1H); 8.31 (d,2H); 8.14 (d,1H); 8.08 (s,1H); 8.04 (d,1H); 7.82 (dd,1H); 7.64-7.51 (m,4H); 7.47 (d,2H); 7.37 (dd,2H); 7.27 (dd,1H); 5.10 (dd,1H); 4.81 (d,1H); 4.13 (dq,1H); 1.18 (d,3H).
18	Calcd. C,78.76; H,6.10; N,7.07 Found C,78.60; H,6.08; N,7.00	3260; 3220; 1632; 1550 *	396 (M+.); 367; 262; 219	9.24 (d,1H); 8.07 (d,1H); 7.97 (dd,2H); 7.76-7.70 (m,1H); 7.62-7.51 (m,5H); 7.46 (d,2H); 7.39 (dd,2H); 7.29 (dd,1H); 5.10 (dt,1H); 3.52 (s,3H); 1.82 (dq,2H); 1.00 (t,3H).
19	Calcd. C,82.43; H,7.16; N,6.63 Found C,82.31; H,7.20; N,6.58	3240; 1630; 1540	423 (MH+) •	(353 K): 8.89 (d br,1H); 8.00 (d,1H); 7.70 (dd,1H); 7.60-7.42 (m,9H); 7.36 (dd,2H); 7.28 (dd,1H); 5.13 (dt,1H); 2.66 (m,2H); 1.90 (ddq,2H); 1.30 (m,2H); 1.00 (t,3H); 0.95 (m,2H); 0.57 (t br,3H).
20	Calcd. C,77.04; H,5.54; N,6.42 Found C,76.81; H,5.54; N,6.35	3290; 1760; 1645; 1590; 1532	436 (M+.); 377; 272; 271	(353 K): 9.50 (d,1H); 8.08 (d,1H); 7.88 (d,1H); 7.80-7.72 (m,2H); 7.60 (dd,1H); 7.52 (dd,2H); 7.47-7.30 (m,6H); 5.90 (d,1H); 2.60 (t,2H); 2.57 (t,2H); 2.26-2.06 (m,2H).

Ex.	Elemental analysis	IR (KBr); cm^{-1}	MS (EI; source 200°C; 70 eV; 200 μA)	300 MHz ^1H NMR (DMSO), 303 K
21	Calcd. C,82.63; H,7.61; N,6.22 Found C,82.84; H,7.64; N,6.16	3270; 1635; 1550 *	450 (M+.); 421; 316	(373 K): 8.71 (d br,1H); 7.99 (d,1H); 7.70 (m,2H); 7.52-7.42 (m,8H); 7.37 (dd,2H); 7.27 (dd,1H); 5.12 (dt,1H); 2.67 (dd,2H); 1.91 (ddq,2H); 1.36-1.26 (m,2H); 1.12-1.02 (m,2H); 1.00 (t,3H); 1.00-0.90 (m,4H); 0.76 (t,3H).
22	Calcd. C,82.07; H,6.36; N,7.36 Found C,81.95; H,6.33; N,7.30	3260; 1630; 1535	380 (M+.); 351; 246; 218	(353 K): 8.90 (d br,1H); 8.01 (d,1H); 7.72 (dd,1H); 7.65 (d br,1H); 7.60-7.49 (m,6H); 7.46 (d,2H); 7.38 (dd,2H); 7.24 (dd,1H); 5.12 (dt,1H); 2.30 (s,3H); 1.98-1.78 (m,2H); 0.99 (t,3H).
23	Calcd. C,82.07; H,6.36; N,7.36 Found C,81.80; H,6.37; N,7.30	3260; 1630; 1535	380 (M+.); 351; 246; 218	(353 K): 8.90 (d br,1H); 8.01 (d,1H); 7.72 (dd,1H); 7.65 (d br,1H); 7.60-7.49 (m,6H); 7.46 (d,2H); 7.38 (dd,2H); 7.24 (dd,1H); 5.12 (dt,1H); 2.30 (s,3H); 1.98-1.78 (m,2H); 0.99 (t,3H).
24	Calcd. C,73.22; H,5.20; N,6.57 Found C,72.88; H,5.25; N,6.44	3282; 1750; 1640; 1530	426 (M+.); 367; 277	9.65 (d,1H); 8.18 (d,1H); 8.11 (d,1H); 7.96 (s,1H); 7.83 (dd,1H); 7.81 (dd,1H); 7.66 (dd,1H); 7.54-7.46 (m,3H); 7.44-7.33 (m,3H); 7.22 (d,1H); 7.13 (dd,1H); 5.80 (d,1H); 3.87 (s,1H); 3.71 (s,3H).
25	Calcd. C,84.13; H,5.92; N,6.33 Found C,82.28; H,5.86; N,6.19	3250; 1630; 1545	442 (M+.); 413; 308; 280	8.86 (d,1H); 8.13 (d,1H); 7.83 (dd,1H); 7.71-7.59 (m,2H); 7.31-7.14 (m,12H); 7.04 (d br,2H); 4.75 (dt,1H); 1.58-1.42 (m,2H); 0.63 (t br,3H).
26	Calcd. C,72.45; H,4.62; N,6.76 Found C,72.19; H,4.66; N,6.69	3320; 1745; 1650; 1595	414 (M+.); 355; 250; 222	9.70 (d,1H); 8.21 (d,1H); 8.16 (d,1H); 8.07 (dd,1H); 7.90 (d,1H); 7.86 (dd,1H); 7.72 (dd,1H); 7.64-7.55 (m,1H); 7.51 (dd,1H); 7.45-7.34 (m,4H); 5.80 (d,1H); 3,75 (s,3H).

Ex.	Elemental analysis	IR (KBr); cm^{-1}	MS (EI; source 200°C; 70 eV; 200 μA)	300 MHz ^1H NMR (DMSO), 303 K
27	Calcd. C,69.03; H,4.62; N,6.44 Found C,68.97; H,4.63; N,6.43	3250; 1650; 1585; 1550	434 (M+.); 405; 232; 204	9.50 (d,1H); 8.31 (d,2H); 8.15 (d,1H); 8.10 (s,1H); 8.00 (d,1H); 7.81 (dd,1H); 7.72 (d,1H); 7.66 (d,1H); 7.64-7.52 (m,4H); 7.46 (dd,1H); 4.11 (dt,1H); 1.83 (dq,2H); 0.98 (t,3H).
28	Calcd. C,78.24; H,5.47; N,7.60 Found C,78.49; H,5.58; N,7.41	3260; 1645; 1590; 1550	368 (M+.); 337; 232; 204	9.22 (d,1H); 8.33 (d,2H); 8.18 (s,1H); 8.13 (d,2H); 7.81 (dd,1H); 7.64-7.51 (m,4H); 7.46 (d,2H); 7.37 (dd,2H); 7.28 (dd,1H); 5.21 (dt,1H); 5.05 (t,1H); 3.71 (dd,2H).
29	Calcd. C,81.93; H,6.05; N,7.64 Found C,81.79; H,6.06; N,7.62	3260; 1650; 1595; 1550	366 (M+.); 337; 232; 204	9.24 (d,1H); 8.30 (d,2H); 8.14 (d,1H); 8.09 (s,1H); 8.02 (d,1H); 7.82 (dd,1H); 7.63-7.51 (m,4H); 7.46 (d,2H); 7.38 (dd,2H); 7.24 (dd,1H); 5.14 (dt,1H); 1.95-1.78 (m,2H); 0.98 (t,3H).
30	Calcd. C,76.08; H,5.40; N,6.83 Found C,75.88; H,5.37; N,7.08	3260; 1755; 1735; 1640; 1580; 1530	410 (M+.); 351; 261; 246; 217	9.70 (d,1H); 8.02 (d,1H); 7.76 (dd,1H); 7.70-7.47 (m,9H); 7.47-7.34 (m,3H); 6.82 (d,1H); 3.75 (s,3H); 2.32 (s br,3H).
31	Calcd. C,82.08; H,6.36; N,7.36 Found C,81.82; H,6.34; N,7.33	3220; 1630; 1550	380 (M+.); 351; 246; 217	(353 K): 9.00 (d,1H); 8.01 (d,1H); 7.37 (dd,1H); 7.60-7.48 (m,7H); 7.45 (d,2H); 7.38 (dd,2H); 7.28 (dd,1H); 5.10 (dt,1H); 2.28 (s,3H); 2.00-1.80 (m,2H); 1.00 (t,3H).
32	Calcd. C,69.69; H,4.45; N,6.50 Found C,69.58; H,4.49; N,6.49	3270; 1750; 1670; 1595; 1520	430 (M+.); 371;266; 238; 203	9.78 (d,1H); 8.29 (d,2H); 8.24 (d,1H); 8.19 (d,1H); 8.16 (s,1H); 7.73 (dd,1H); 7.61-7.49 (m,5H);7.47-7.36 (m,3H); 5.80 (d,1H); 3.79 (s,3H).
33	Calcd. C,76.49; H,5.40; N,6.82 Found C,76.74; H,5.40; N,6.88	3240; 1750; 1665; 1590; 1510; 1500	410 (M+.); 351; 246; 218	9.70 (d,1H); 8.26 (d,2H); 8.08 (s,1H); 8.03 (d,1H); 7.96 (s,1H); 7.68 (dd,1H); 7.60-7.50 (m,5H); 7.48-7.36 (m,3H); 5.80 (d,1H); 3.79 (s,3H); 2.50 (s,3H).

Ex.	Elemental analysis	IR (KBr); cm^{-1}	MS (EI; source 200°C; 70 eV; 200 μA)	300 MHz ^1H NMR (DMSO), 303 K
34	Calcd. C,78.51; H,5.79; N,7.32, Found C,78.78; H,5.78; N,7.23	3220; 1740; 1695; 1535	382 (M+.); 337; 232; 204	9.35 (d,1H); 8.32 (d,2H); 8.14 (d,1H); 8.11 (d,1H); 8.10 (s,1H); 7.84 (dd,1H); 7.64 (dd,1H); 7.61-7.54 (m,3H); 7.50 (d,2H); 7.40 (dd,2H); 7.30 (dd,1H); 5.41 (dt,1H); 3.73-3.60 (m,2H); 3.36 (s,3H).
35	Calcd. C,69.69; H,4.45; N,6.50 Found C,70.27; H,4.46; N,6.45	3240; 1750; 1670; 1590; 1550; 1500	430 (M+.); 371; 266; 238; 203	9.80 (d,1H); 8.29 (d,2H); 8.27 (d,1H); 8.21 (s,1H); 8.16 (d,1H); 7.86 (dd,1H); 7.61-7.51 (m,5H); 7.48-7.38 (m,3H); 5.80 (d,1H); 3.75 (s,3H).
36	Calcd. C,76.40; H,5.70; N,6.60 Found C,76.44; H,5.72; N,6.62	3240; 1760; 1640; 1540	425 (MH+) •	(353 K): 9.52 (d,1H); 8.01 (d,1H); 7.89 (s br,1H); 7.74 (dd,1H); 7.60 (dd,1H); 7.54-7.48 (m,7H); 7.44-7.33 (m,3H); 4.88 (d,1H); 3.78 (s,3H); 2.91-2.68 (m,2H); 0.91 (t,3H).
37	Calcd. C,82.08; H,6.36; N,7.36 Found C,82.21; H,6.39; N,7.34	3300; 1635; 1590; 1545	380 (M+.); 337; 232; 204	9.28 (d,1H); 8.14 (d,1H); 8.07 (s,1H); 8.01 (d,1H); 7.82 (dd,1H); 7.64-7.51 (m,4H); 7.46 (d,2H); 7.39 (dd,2H); 7.28 (dd,1H); 5.15 (dt,1H); 1.94-1.69 (m,2H); 1.54-1.29 (m,2H); 0.95 (t,3H).
38	Calcd. C,82.20; H,6.64; N,7.10 Found C,82.34; H,6.64; N,7.07	3240; 1640; 1550	395 (MH+); CI; gas reagent methane; P 5000 mTorr; source 150 °C	(353 K): 8.91 (d,1H); 8.00 (d,1H); 7.71 (dd,1H); 7.68-7.48 (m,7H); 7.45 (d,2H); 7.39 (dd,2H); 7.29 (dd,1H); 5.11 (dt,1H); 2.78-2.62 (m,2H); 2.00-1.80 (m,2H); 1.00 (t,3H); 0.90 (t br,3H).
39	Calcd. C,77.48; H,4.93; N,8.21 Found C,77.25; H,4.99; N,8.07	3330; 1790; 1720; 1665; 1530	511 (M+.); 482; 377; 349; 321	(353 K): 8.90 (d,1H); 8.20 (d,1H); 7.94 (dd,1H); 7.88-6,90 (m,5H); 7.74 (d,1H); 7.69 (dd,1H); 7.48-7.42 (m,2H); 7.36-7.31 (m,3H); 7.25-7.20 (m,2H); 7.18-7.10 (m,2H); 4.85 (dt,1H); 1.73 (ddq,1H); 0.82 (t,3H).

Ex.	Elemental analysis	IR (KBr); cm^{-1}	MS (EI; source 200°C; 70 eV; 200 μA)	300 MHz ^1H NMR (DMSO), 303 K
40	Calcd. C,82.32; H,6.91; N,6.86 Found C,82.02; H,6.95; N,6.90	3250; 1635; 1550	408 (M+.); 379, 289, 274; 246	(373 K): 8.72 (d,1H); 8.00 (d,1H); 7.70 (dd,1H); 7.55-7.42 (m,9H); 7.38 (dd,2H); 7.28 (dd,1H); 5.15 (dt,1H); 2.66 (dd,2H); 1.94 (ddq,2H); 1.33 (m,2H); 1.01 (t,3H); 0.56 (t,3H).
41	Calcd. C,58.02; H,4.12; N,5.20; Br,29.69 Found C,58.14; H,4.18; N,5.22; Br,29.44	3250; 1650; 1540	537/539/541 (MH+) •	(353 K): 8.95 (d,1H); 7.96 (d,1H); 7.83 (dd,1H); 7.76 (d,1H); 7.71 (d,2H); 7.55 (d,2H); 7.45 (dd,2H); 7.39 (dd,2H); 7.30 (dd,1H); 5.10 (dt,1H); 2.92 (s,3H); 2.30 (s,3H); 1.88 (ddq,2H); 1.01 (t,3H).
42	Calcd. C,67.98; H,5.04; N,6.10; Br,17.39 Found C,68.04; H,5.02; N,6.05; Br,17.26	3260; 1640; 1540	459/461 (MH+) •	(353 K): 8.94 (d br,1H); 7.96 (d,1H); 7.81 (dd,1H); 7.76 (d,1H); 7.60-7.49 (m,4H); 7.45 (d,2H); 7.40 (dd,2H); 7.30 (dd,1H); 5.10 (dt,1H); 2.30 (s,3H); 1.89 (ddq,2H); 1.01 (t,3H).
43	Calcd. C,73.22; H,5.20; N,6.57 Found C,73.41; H,5.39; N,6.61	3200; 1750; 1665; 1620; 1520	426 (M+.); 367; 262; 234	9.70 (d,1H); 8.24 (d,2H); 8.08 (s,1H); 8.05 (d,1H); 7.61 (d,1H); 7.58-7.35 (m,9H); 5.80 (d,1H); 3.89 (s,3H); 3.74 (s,3H).
44	Calcd. C,74.30; H,4.62; N,6.42 Found C,74.28; H,4.61; N,6.41	3200; 1750; 1660; 1590; 1550; 1525; 1500	436 (M+.); 337; 272; 244	9.80 (d,1H); 8.18 (d,1H); 8.11 (d,1H); 8.09 (s,1H); 7.90 (s,1H); 7.87 (dd,1H); 7.80 (d,1H); 7.77 (d,1H); 7.67 (dd,1H); 7.54 (d,2H); 7.47-7.31 (m,5H); 5.80 (d,1H); 3.78 (s,3H).
45	Calcd. C,84.08; H,5.65; N,6.54 Found C,84.13; H,5.65; N,6.51	3320; 1635; 1590; 1530	337 (M-C_7H_7)+; 232; 204; 91	9.32 (ABXY,1H); 8.22 (d,2H); 8.09 (d,1H); 7.78 (dd,1H); 7.77 (s,1H); 7.64-7.52 (m,6H); 7.50-7.28 (m,9H); 5.53 (ABXY,1H); 3.20 (ABXY,1H); 3.16 (ABXY,1H).

Ex.	Elemental analysis	IR (KBr); cm^{-1}	MS (EI; source 200°C; 70 eV; 200 μA)	300 MHz ^{1}H NMR (DMSO), 303 K
46	Calcd. C,70.91; H,4.22; N,6.89; F,14.02 Found C,70.86; H,4.17; N,6.92; F,13.88	3300; 1655; 1590; 1540; 1500	406 (M+.); 386; 232; 204	10.15 (d,1H); 8.30 (dd,2H); 8.18 (d,1H); 8.10 (s,1H); 7.98 (d,1H); 7.86 (dd,1H); 7.75-7.42 (m,9H); 6.21 (m,1H).
47	Calcd. C,78.74; H,6.10; N,7.06 Found C,78.72; H,6.10; N,7.01	3250; 1635; 1550; 1500	396 (M+.); 367; 262; 219	9.24 (d,1H); 8.07 (d,1H); 7.97 (dd,2H); 7.76-7.70 (m,1H); 7.62-7.51 (m,5H); 7.46 (d,2H); 7.39 (dd,2H); 7.29 (dd,1H); 5.10 (dt,1H); 3.52 (s,3H); 1.82 (dq,2H); 1.00 (t,3H).
48	Calcd. C,82.18; H,6.64; N,7.10 Found C,81.93; H,6.64; N,7.05	3250; 1630; 1540; 1500	394 (M+.); 365; 275; 260	(353 K): 8.90 (d br,1H); 8.00 (d,1H); 7.70 (dd,1H); 7.56-7.42 (m,9H); 7.38 (dd,2H); 7.29 (dd,1H); 5.13 (dt,1H); 2.72 (m,2H); 1.90 (ddq,2H); 1.00 (t,3H); 0.90 (t br,3H).
49	Calcd. C,74.90; H,5.28; N,6.99; Found C,74.67; H,5.33; N,7.03;	3270; 1645; 1590; 1550; 1495; 770	400 (M+.); 371; 232; 204	9.20 (d,1H); 8.32 (d,2H); 8.08 (dd,2H); 8.06 (s,1H); 7.82 (t,1H); 7.65-7.40 (m,8H); 5.00 (dt,1H); 1.93-1.73 (m,2H); 0.98 (t,3H).
50	Calcd. C,76.08; H,5.40; N,6.82 Found C,76.16; H,5.42; N,6.84	1750; 1640; 1595;1550	411 (MH+); 232; 204•	8.32 (d,2H); 8.16 (d,1H); 8.10 (s,1H); 7.88 (dd,1H); 7.71 (dd,1H); 7.60-7.42 (m,9H); 3.86 (s,3H); 2.56 (s,3H).
51	Calcd. C,68.64; H,4.51; N,6.96 Found C,68.52; H,4.53; N,6.94	3290; 1740; 1640; 1590; 1530	402 (M+.); 343; 238; 210	9.72 (d,1H); 8.47 (dd,1H); 8.15 (d,1H); 8.07 (d,1H); 8.05 (s,1H); 7.96 (dd,1H); 7.81 (dd,1H); 7.71 (dd,1H); 7.62 (dd,1H); 7.53 (d,2H); 7.46-7.36 (m,3H); 5.78 (d,1H); 3.78 (s,3H).
52	Calcd. C,76.76; H,5.25; N,6.63 Found C,76.39; H,5.25; N,6.55	3250; 1750; 1660; 1590; 1520	422 (M+.); 258; 230	9.70 (d,1H); 8.45 (dd,1H); 8.18 (d,1H); 7.80-7.38 (m,11H); 5.83 (d,1H); 3.79 (s,3H); 3.20-2.80 (s br,4H).

Ex.	Elemental analysis	IR (KBr); cm^{-1}	MS (EI; source 200°C; 70 eV; 200 μA)	300 MHz ^1H NMR (DMSO), 303 K
53	Calcd. C,71.68; H,4.97; N,10.90 Found C,71.39; H,4.99; N,10.81	3410; 3250; 1740; 1678; 1600 *	385 (M+.); 221; 193	11.68 (s br,1H); 9.71 (d,1H); 8.17 (d,1H); 7.99 (d,1H); 7.86 (s,1H); 7.66 (dd,1H); 7.58-7.35 (m,6H); 7.00 (s br,2H); 6.22 (s br,1H); 5.75 (d,1H); 3.73 (s,3H).
54	Calcd. C,65.50; H,4.25; N,10.42 Found C,65.48; H,4.22; N,10.38	3300; 1755; 1645; 1585; 1530	344 (M-$COOCH_3$)+; 239; 211	9.82 (d,1H); 8.28 (s,1H); 8.19 (d,1H); 8.14 (d,1H); 8.10 (d,1H); 8.00 (d,1H); 7.88 (dd,1H); 7.73 (dd,1H); 7.53 (d,2H); 7.47-7.36 (m,3H); 5.80 (d,1H); 3.78 (s,3H).
55	Calcd. C,82.39; H,5.53; N,7.69 Found C,82.31; H,5.52; N,7.65	3240; 1640; 1590; 1545	365 (MH)+ •	9.20 (d,1H); 8.31 (d,2H); 8.27 (d,1H); 8.16 (s,1H); 8.14 (d,1H); 7.85 (dd,1H); 7.68 (dd,1H); 7.62-7-46 (m,4H); 7.32-7.23 (m,3H); 5.69 (dt,1H); 3.08-2.85 (m,2H); 2.64-2.52 (m,1H); 2.10-1.96 (m,1H).
56	Calcd. C,82.20; H,6.64; N,7.10 Found C,82.29; H,6.66; N,7.05	3270; 1640; 1590; 1540	394 (M+.); 337; 232; 204	9.12 (d,1H); 8.30 (d,2H); 8.14 (d,1H); 8.07 (s,1H); 8.02 (d,1H); 7.82 (dd,1H); 7.64-7.52 (m,4H); 7.46 (d,2H); 7.39 (dd,2H); 7.28 (dd,1H); 5.13 (dt,1H); 1.96-1.71 (m,2H); 1.48-1.27 (m,4H); 0.9 (t,3H).
57	Calcd. C,76.08; H,5.40; N,6.82 Found C,75.92; H,5.44; N,6.77	3300; 1752; 1642; 1590; 1530	410 (M+.); 351; 246; 218; 203	9.74 (d,1H); 8.20 (d,2H); 8.18 (d,1H); 8.12 (d,1H); 8.08 (s,1H); 7.82 (dd,1H); 7.64 (dd,1H); 7.54 (d,2H); 7.47-7.36 (m,5H); 5.8 (d,1H); 3.79 (s,3H); 2.40 (s,3H).

Ex.	Elemental analysis	IR (KBr); cm^{-1}	MS (EI; source 200°C; 70 eV; 200 μA)	300 MHz ^1H NMR (DMSO), 303 K
58	Calcd. C,82.53; H,7.39; N,6.42 Found C,82.59; H,7.45; N,6.39	3260; 1650; 1590; 1550; 1540	337 (M-C_7H_{15})+; 249; 232; 204	9.28 (d,1H); 8.29 (d,2H); 8.14 (d,1H); 8.07 (s,1H); 8.02 (d,1H); 7.82 (dd,1H); 7.64-7.52 (m,4H); 7.46 (d,2H); 7.38 (dd,2H); 7.28 (dd,1H); 5,14 (dt,1H); 1.98-1.71 (m,2H); 1.30-1.20 (m,10H); 0.86 (t br,3H).
59	Calcd. C,76.08; H,5.40; N,6.82 Found C,76.21; H,5.40; N,6.79	3400-3100; 1742; 1665; 1590; 1530	410 (M+.); 261; 218	9.70 (d,1H); 8.22 (d,1H); 8.10 (d,1H); 7.84 (dd,1H); 7.70 (dd,1H); 7.67 (s,1H); 7.56 (d,1H); 7.50 (dd,2H); 7.45-7.33 (m,5H); 5.80 (d,1H); 3.78 (s,3H); 2.42 (s,3H).
60	Calcd. C,73.22; H,5.20; N,6.57 Found C,72.89; H,5.20; N,6.48	3300; 1750; 1645; 1590; 1520	426 (M+.); 367; 262; 234; 219; 191	9.72 (d,1H); 8.25 (d,2H); 8.17 (d,1H); 8.09 (d,1H); 8.07 (s,1H); 7.80 (dd,1H); 7.62 (dd,1H); 7.54 (dd,2H); 7.46-7.36 (m,3H); 7.12 (d,2H); 5.80 (d,1H); 3.89 (s,3H); 3.75 (s,3H).
61	Calcd. C,82.62; H,6.16; N,7.14 Found C,82.76; H,6.18; N,7.19	3230; 1640; 1590; 1550 *	392 (M+.); 249; 232, 204	9.00 (s,1H); 8.32 (dd,2H); 8,13 (d,1H); 8.05 (s,1H); 7.93 (d,1H); 7.81 (dd,1H); 7.64-7.52 (m,6H); 7.39 (dd,2H); 7.26 (dd,1H); 2.61-2.50 (m,2H); 2.10-2.00 (m,2H); 2.00-1.75 (m,4H).
62	Calcd. C,72.80; H,4.89; N,6.79 Found C,72.86; H,4.91; N,6.75	3500-3100; 1750; 1670; 1640; 1590	412 (M+.); 353; 248; 220	9.90 (s,1H); 9.70 (d,1H); 8.14 (d,2H): 8.14 (d,1H); 8.06 (d,1H); 8.01 (s,1H); 7.78 (dd,1H); 7.60 (dd,1H); 7.53 (dd,2H); 7.46-7.35 (m,3H); 6.94 (d,2H); 5.80 (d,3H); 3.75 (s,3H).
63	Calcd. C,70.90; H,4.58; N,6.36 Found C,70.73; H,4.59; N,6.35	3350; 1735; 1655; 1590	440 (M+.); 381; 276; 248	9.70 (d,1H); 8.17 (d,1H); 8.09 (d,1H); 8.06 (s,1H): 7.88 (d,1H); 7.85 (dd,1H); 7.80 (dd,1H); 7.62 (dd,1H); 7.42 (dd,2H); 7.46-7.36 (m,3H); 7.10 (d,2H); 6.13 (s,2H); 5.73 (d,1H); 3.73 (s.3H).

Ex.	Elemental analysis	IR (KBr); cm^{-1}	MS (EI; source 200°C; 70 eV; 200 μA)	300 MHz ^1H NMR (DMSO), 303 K
64	Calcd. C,81.94; H,6.05; N,7.64 Found C,82.02; H,6.07; N,7.60	3220; 1640; 1590; 1545	366 (M+.); 351; 248; 232; 204	9.01 (s br,1H); 8.34 (dd,2H); 8.15 (s,1H); 8.13 (d,1H); 8.01 (d,1H); 7.81 (dd,1H); 7.66-7.52 (m,6H); 7.39 (dd,2H); 7.25 (dd,1H).
65	Calcd. C,82.07; H,6.36; N,7.36 Found C,82.15; H,6.36; N,7.41	3320; 1640; 1590; 1530	380 (M+.); 351; 232; 204	9.20 (d,1H); 8.29 (dd,2H); 8.14 (d,1H); 8.06 (s,1H); 8.03 (d,1H); 7.81 (dd,1H); 7.64-7.50 (m,4H); 7.34 (d,2H); 7.19 (d,2H); 5.00 (dt,1H); 2.30 (s,3H); 1.93-1.73 (m,2H); 0.98 (t,3H).
66	Calcd. C,71.68; H,4.97; N,10.90 Found C,70.42; H,4.99; N,10.56	3360; 3240; 1750; 1630; 1600; 1560	385 (M+.); 326; 221; 193	11.20 (s br,1H); 9.65 (d,1H); 8.05 (d,1H); 7.93 (d,1H); 7.78 (s,1H); 7.70 (dd,1H); 7.67 (m,1H); 7.55-7.34 (m,6H); 6.87 (m,1H); 6.80 (m,1H); 6.77 (d,1H); 3.75 (s,3H).
67	Calcd. C,64.53; H,3.90; N,6.02; Cl,15.24 Found C,64.59; H,3.95; N,5.94; Cl,15.03	3200; 1755; 1635; 1590; 1535	464 (M+.); 405; 300; 272; 237	9.70 (d,1H); 8.55 (d,1H); 8.30 (dd,1H); 8.22 (d,1H); 8.21 (s,1H); 8.17 (d,1H); 7.86 (dd,1H); 7.84 (d,1H); 7.70 (dd,1H); 7.54 (dd,2H); 7.47-7.36 (m,3H); 5.78 (d,1H); 3.74 (s,3H).
68		3300; 1635; 1590; 1530; 1495; 770	338; 337; 255; 233; 232; 204	9.18 (d br,1H); 8.35 (d,2H); 8.20 (s,1H); 8.13 (d,1H); 8.07 (d,1H); 7.81 (dd,1H); 7.63-7.51 (m,4H); 7.44 (d,2H); 7.38 (dd,2H); 7.28 (dd,1H); 5.08 (dt br,1H); 2.89 (d,2H); 1.60 (s br,2H).
69	Calcd. C,78.71; H,6.08; N,11.01 Found C,78.45; H,6.10; N,10.96	3490; 3380; 3260; 1630; 1600	381 (M+.); 352;247; 219; 218	9.20 (d,1H); 7.87 (m,1H); 7.70 (d,2H); 7.59-7.26 (m,11H); 5.08 (dt,1H); 4.80 (s br, 2H); 2.81 (dq,2H); 0.95 (t,3H).

Ex.	Elemental analysis	IR (KBr); cm^{-1}	MS (EI; source 200°C; 70 eV; 200 μA)	300 MHz ^1H NMR (DMSO), 303 K
70	Calcd. C,74.90; H,5.28; N,6.99; Cl,8.84 Found C,74.88; H,5.25; N,6.98; Cl,8.92	3230; 1640; 1550	400 (M+.); 371; 266; 238; 203	9.37 (d,1H), 8.10 (d,1H); 7.85 (dd,1H); 7.75-7.35 (m,12H); 5.07 (dt,1H);1.80 (dq,2H); 0.98 (t,,3H).
71	Calcd. C,67.42; H,4.75; N,6.29; Br,17.94 Found C,67.57; H,4.80; N,6.31; Br,18.00	3240; 1640; 1545	444/446 (M+.); 415/417; 310/312; 203	9.35 (d,1H); 8.10 (d,1H); 7.85 (dd br,1H); 7.70-7.30 (m,12H); 5.05 (dt,1H); 1.81 (dq,2H); 0.99 (t,3H).
72	Calcd. C,82.07; H,6.36; N,7.36 Found C,82.00; H,6.36; N,7.33	3240; 1630;1590; 1545	381 (MH)+ ; TSP, ammonium acetate (50 mM)/acetonitrile 60 : 40 as eluent; source 250 °C	9.24 (d,1H); 8.29 (d,2H); 8.14 (d,1H); 8.01 (s,1H); 7.96 (d,1H); 7.81 (dd,1H); 7.64-7.51 (m,4H); 7.47-7.36 (m,4H); 7.29 (dd,1H); 4.90 (dd,1H); 2.19-2.02 (m,1H);1.08 (d,3H); 0.80 (d,3H).
73	Calcd. C,81.94; H,6.05; N,7.64 Found C,79.33; H,5.82; N,7.34	3320; 1635; 1590; 1535	366 (M+.); 337; 232; 204	9.24 (d,1H); 8.30 (d,2H); 8.14 (d,1H); 8.09 (s,1H); 8.02 (d,1H); 7.82 (dd,1H); 7.63-7.51 (m,4H); 7.46 (d,2H); 7.38 (dd,2H); 7.24 (dd,1H); 5.14 (dt,1H); 1.95-1.78 (m,2H); 0.98 (t,3H).
74	Calcd. C,81.94; H,6.05; N,7.64 Found C,82.08; H,6.09; N,7.59	3280; 1637; 1590; 1540	366 (M+.); 337; 232; 204	9.24 (d,1H); 8.30 (d,2H); 8.14 (d,1H); 8.09 (s,1H); 8.02 (d,1H); 7.82 (dd,1H); 7.63-7.51 (m,4H); 7.46 (d,2H); 7.38 (dd,2H); 7.24 (dd,1H); 5.14 (dt,1H); 1.95-1.78 (m,2H); 0.98 (t,3H).
75	Calcd. C,72.45; H,4.62; N,6.76 Found C,72.28; H,4.59; N,6.79	3280; 1740; 1650; 1630; 1550	414 (M+.); 355; 250; 222	9.75 (d,1H); 8.28 (dd,2H); 8.21 (dd,1H); 8.2 (s,1H); 7.95 (dd,1H); 7.77 (ddd,1H); 7.61-7.50 (m,5H); 7.47-7.36 (m,3H); 5.80 (d,1H); 3.74 (s,3H).

Ex.	Elemental analysis	IR (KBr); cm^{-1}	MS (EI; source 200°C; 70 eV; 200 μA)	300 MHz ^1H NMR (DMSO), 303 K
76	Calcd. C,74.60; H,6.51; N,6.96 Found C,74.32; H,6.50; N,6.90	1740; 1665; 1595; 1535	402 (M+.); 238; 210	9.61 (d,1H); 8.11 (d,1H); 7.99 (d,1H); 7.75 (dd,1H); 7.59 (dd,1H); 7.50 (d,2H); 7.47-7.35 (m,4H); 5.74 (d,1H); 3.72 (s,3H); 2.90 (tt,1H); 2.00-1.20 (m,10H).
77	Calcd. C,69.69; H,4.45; N,6.50 Found C,69.81; H,4.45; N,6.54	3290; 1745; 1660; 1640; 1585; 1530	431 (MH+) •	9.71 (d,1H); 8.37 (s,1H); 8.30-8.15 (m,3H); 7.85 (dd,1H); 7.69 (dd,1H); 7.63-7.38 (m,8H); 5.79 (d,1H); 3.74 (s,3H).
78	Calcd. C,69.69; H,4.44; N,6.50 Found C,69.90; H,4.42; N,6.57	3290; 1745; 1660; 1600; 1520	431(MH+); TSP, ammonium acetate (0.1 M)/acetonitrile 60 : 40 as eluent; source 250 °C	9.70 (d,1H); 8.24 (d,1H); 8.14 (d,1H); 7.87 (dd,1H); 7.77 (s,1H); 7.76-7.62 (m,3H); 7.58-7.48 (m,4H); 7.44-7.34 (m,3H); 5.80 (d,1H); 3.72 (s,3H).
79	Calcd. C,78.51; H,5.80; N,7.32 Found C,78.55; H,5.82; N,7.26	3310; 3110; 1645; 1575; 1535	382 (M+.); 353; 264; 247; 219	9.80 (s,1H); 9.11 (d,1H); 8.00-7.94 (m,3H); 7.61-7.42 (m,8H); 7.38 (dd,2H); 7.28 (dd,1H); 5.06 (dt,1H); 1.82 (ddq,2H); 0.97 (t,3H).
80	Calcd. C,71.36; H,4.88; N,6.16 Found C,71.39; H,4.88; N,6.17	3320; 1760; 1735; 1650; 1530	455 (MH)+ •	9.74 (d,1H); 8.24 (dd,2H); 8.17 (s,1H); 8.08 (dd,1H); 7.70-7.50 (m,7H); 7.46-7.35 (m,3H); 5.75 (d,1H); 3.75 (s,3H).
81	Calcd. C,72.80; H,4.89; N,6.79 Found C,73.24; H,5.00; N,6.42	3360; 3300; 1745; 1650; 1600; 1560;	413 (MH)+ •	9,69 (d,1H); 9.68 (s,1H); 8.49 (d,2H); 8.12 (s,1H); 7.64-7.35 (m,10H); 7.18 (d,1H); 5.79 (d,1H); 3.77 (s,3H).
82	Calcd. C,64.53; H,3.90; N,6.02 Found C,64.71; H,3.96; N,6.00	3240; 1740; 1645; 1595; 1550	464 (M+.); 405; 300; 272; 237	10.68 (d,1H); 8.25 (d,1H); 8.14 (d,1H); 7.88 (dd,1H); 7.82 (d,1H); 7.78 (s,1H); 7.74 (dd,1H); 7.74 (d,1H), 7.62 (dd,1H); 7.51 (d,2H); 7.44-7.33 (m,3H); 6.78 (d,1H); 3.74 (s,3H).

Ex.	Elemental analysis	IR (KBr); cm^{-1}	MS (EI; source 200°C; 70 eV; 200 μA)	300 MHz ^1H NMR (DMSO), 303 K
83	Calcd. C,66.89; H,4.72; N,6.24; Cl,7.90 Found C,66.53; H,4.74; N,6.10; Cl,7.48	3180; 1750; 1660; 1645; 1610; 1535; 1510	412 (M+.); 353; 232; 204	9.62 (d,1H); 8.28 (d,2H); 8.22 (d,1H); 8.16 (d,1H); 8.11 (s,1H); 7.86 (dd,1H); 7.68 (dd,1H); 7.61-7.51 (m,3H); 7.30 (d,2H); 6.80 (d,2H); 5.61 (d,1H); 3.71 (s,3H).
84	Calcd. C,84.03; H,5.35; N,6.76 Found C,83.27; H,5.64; N,7.05	3210; 1640; 1590; 1525	414 (M+.); 337; 232; 204	9.79 (d,1H); 8.30 (dd,2H); 8.15 (s,1H); 8.12 (d,1H); 8.02 (d,1H); 7.81 (dd,1H); 7.63-7.26 (m,14H); 6.52 (d,1H).
85	Calcd. C,78.51; H,5.80; N,7.33 Found C,78.55; H,5.84; N,7.30	3270; 1650; 1630; 1570; 1535	382 (M+.); 264; 247; 219	9.80 (s,1H); 9.11 (d,1H); 8.00-7.94 (m,3H); 7.61-7.42 (m,8H); 7.38 (dd,2H); 7.28 (dd,1H); 5.06 (dt,1H); 1.82 (ddq,2H); 0.97 (t,3H).
86	Calcd. C,72.80; H,4.89; N,6.79 Found C,72.12; H,4.88; N,6.63	3360; 1735; 1625; 1530	412 (M+.); 353; 248; 219	9.85 (s,1H); 9.63 (d br,1H); 7.97 (m,3H); 7.89 (d br,1H); 7.62-7.34 (m,10H); 5.75 (d,1H); 3.76 (s,3H).
87	Calcd. C,78.96; H,6.37; N,10.62 Found C,78.63; H,6.39; N,10.65	3320; 1640; 1590; 1525; 770	395 (M+.); 232; 204	9.15 (d,1H); 9.30 (d,2H); 9.18 (dd, 2H); 8.06 (s,1H); 7.80 (t,1H); 7.70-7.20 (m, 9H); 5.30 (dt,1H); 2.75 (dd,1H); 2.45 (dd,1H); 2.70 (s,6H).
88	Calcd. C,76.26; H,5.66; N,10.26 Found C,75.74; H,5.66; N,10.06	3280; 1660; 1635; 1590	409 (M+.); 337; 232; 204	9.40 (d,1H); 8.26 (d,2H); 8.22 (d,1H); 8.12 (d,1H); 8.05 (s,1H); 7.81 (dd,1H); 7.62 (dd,1H); 7.59-7.49 (m,5H); 7.43-7.33 (m,3H); 6.15 (d,1H); 3.00 (s,3H); 2.90 (s,3H).

Ex.	Elemental analysis	IR (KBr); cm^{-1}	MS (EI; source 200°C; 70 eV; 200 µA)	300 MHz ^1H NMR (DMSO), 303 K
89	Calcd. C,75.57; H,5.02; N,11.02 Found C,75.23; H,5.12; N,10.88	3360; 3270; 1680; 1650; 1600	381 (M+.); 337; 232; 204	9.40 (d,1H); 8.31 (d,2H); 8,16 (s,1H); 8.15 (d,1H); 8,12 (d,1H); 7.81 (dd,1H); 7.78 (s br,1H); 7.64-7.50 (m,6H); 7.41-7.30 (m,3H); 7.23 (s br,1H); 5.71 (d,1H).
90	Calcd. C,77.22; H,5.79; N,9.65 Found C,76.91; H,5.87; N,9.56	3220; 1660; 1620; 1590	436 (MH+); TSP, ammonium acetate (0.1 M)/acetonitrile 60 : 40 as eluent; source 250° C	9.48 (d,1H); 8.27 (d,2H); 8.23 (d,1H); 8.12 (d,1H); 8.06 (s,1H); 8.02 (dd,1H); 7.63 (dd,1H); 7.60-7.50 (m,5H); 7.45-7.33 (m,3H); 5.92 (d,1H); 3.82-3.71 (m,1H); 3.53-3.26 (m,2H); 3.16-3.08 (m,1H); 1.98-1.68 (m,4H).
91	Calcd. C,68.82; H,4.57; N,6.69; Cl,8.46 Found C,68.42; H,4.60; N,6.56; Cl,8.22	1740; 1670; 1635; 1610; 1540	382 (M+.); 337; 204	9.64 (d,1H); 8.28 (d,2H); 8.22 (d,1H); 8.16 (d,1H); 8.13 (s,1H); 7.84 (dd,1H); 7.66 (dd,1H); 7.62-7.51 (m,5H); 7.46-7.34 (m,3H); 5.70 (d,1H).

* oil mull; • FAB POS, thioglycerol matrix, Xe gas, 8 KeV, source 50 °C.

EXAMPLE 92

(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(p-chlorophenyl)quinoline-4-carboxamide

[0069] 2 g (7.0 mmol) of 2-(p-chlorophenyl)quinoline-4-carboxylic acid and 1.7 ml (15.4 mmol) of N-methylmorpholine were dissolved, under nitrogen athmosphere, in 50 ml of dry THF.
The solution was cooled to -20°C and 0.91 ml (7.0 mmol) of isobutyl chloroformate were added. After 20 minutes, 2.12 g (10.5 mmol) of methyl (R,S) phenylglycinate hydrochloride and 1.3 ml (11.9 mmol) of N-methylmorpholine, dissolved in 30 ml of dry THF, were added and the reation mixture was stirred at room temperature overnight.
5 ml of H_2O were added and the reaction mixture was evaporated *in vacuo* to dryness. The residue was dissolved in Et_2O, washed with a saturated solution of $NaHCO_3$, separated, dried over Na_2SO_4 and evaporated *in vacuo* to dryness. The residual oil was flash chromatographed on 230-400 mesh silica gel, eluting with a mixture of hexane/isopropyl ether 7 : 3 to afford 0.9 g of crude product, which was recrystallized three times with $iPrO_2$/toluene to yield 0.5 g of the title compound.
$C_{25}H_{19}ClN_2O_3$
M.P. = 170-172 °C
M.W. = 430.90

Elemental analysis	Calcd.	C, 69.72;	H, 4.45;	N, 6.50
	Found	C, 69.82;	H, 4.47;	N, 6.48

I.R. (KBr): 3280; 1740; 1670; 1635; 1590; 1530 cm^{-1}.

300 MHz 1H-NMR (DMSO-d6): 9.71 (d, 1H); 8.32 (d, 2H); 8.21 (d, 1H); 8.13 (d, 1H); 8.13 (s, 1H); 7.85 (dd, 1H); 7.67 (dd, 1H); 7.63 (d, 2H); 7.53 (dd, 2H); 7.46-7.38 (m, 3H); 5.79 (d, 1H); 3.74 (s, 3H).

MS (EI; source 200 °C;70 eV; 200 μA): 430 (M+.); 371; 266; 238; 203.

EXAMPLE 93

(R)-N-[α-(Methoxycarbonyl)-4-methoxybenzyl]-2-phenylquinoline-4-carboxamide

[0070] 0.62 g (1.5 mmol) of (R)-N-[α-(methoxycarbonyl)-4-hydroxybenzyl]-2-phenylquinoline-4-carboxamide (compound of Ex. 83) were dissolved in 30 ml of dry acetone and 2 ml of dry DMF; 0.14 g (0.75 mmol) of K_2CO_3 were added and the reaction mixture was stirred for 30 minutes.
0.093 ml (1.5 mmol) of methyl iodide were added at room temperature and the reaction mixture was heated at 40 °C for 4 hours. 0.104 g (0.75 mmol) of K_2CO_3 and 0.093 ml (1.5 mmol) of methyl iodide were added again, and the mixture refluxed for additional 6 hours.
The mixture was evaporated *in vacuo* to dryness, dissolved in EtOAc and washed with H_2O. The organic layer, dried over Na_2SO_4, was evaporated *in vacuo* to dryness. The residue was recrystallized from Et_2O to yield 0.45 g of the title compound.
$C_{26}H_{22}N_2O_4$
M.P. = 160-162 °C
M.W. = 426.48

Elemental analysis	Calcd.	C, 73.22;	H, 5.20;	N, 6.57
	Found	C, 73.01;	H, 5.20;	N, 6.48

I.R. (KBr): 3210; 1750; 1635; 1625; 1590; 1530; 1515 cm^{-1}

300 MHz 1H-NMR (DMSO-d6): 9.65 (d, 1H); 8.28 (d, 2H); 8.21 (d, 1H); 8.14 (d, 1H); 8.10 (s, 1H); 7.84 (dd, 1H); 7.67 (dd, 1H); 7.61-7.49 (m, 3H); 7.44 (d, 2H); 6.98 (d, 2H); 4.70 (d, 1H); 3.79 (s, 3H); 3.76 (s, 3H).

MS (EI; source 200 °C;70 eV; 200 μA): 426 (M+.); 367; 232; 204.

EXAMPLE 94

(R,S)-N-[α-(Methoxycarbonyl)-α-(methyl)benzyl]-N-methyl-2-phenylquinoline-4-carboxamide hydrochloride

[0071] 0.50 g (1.3 mmol) of (R,S)-N-[α-(methoxycarbonyl)benzyl]-2-phenylquinoline-4-carboxamide (compound of Ex. 4) were dissolved, under nitrogen athmosphere, in 10 ml of dry DMF.
The solution was cooled to 0 °C and 0.052 g (1.3 mmol) of NaH (60%) were added; after 20 minutes at 0 °C the temperature was raised to r.t. and 0.09 ml (1.4 mmol) of MeI were added. The reation mixture was stirred at room temperature overnight, then the procedure was repeated by adding additional 0.052 g (1.3 mmol) of NaH (60%) and 0.1 ml (1.6 mmol) of MeI.
After 6 hours at room temperature, 10 ml of saturated solution of NH_4Cl were added and the reaction mixture was evaporated *in vacuo* to dryness. The residue was dissolved in CH_2Cl_2 and washed with water; the organic layer was separated, dried over Na_2SO_4 and evaporated *in vacuo* to dryness.
The residual oil was flash chromatographed on 230-400 mesh silica gel, eluting with a mixture of hexane/ethyl acetate 3 : 2 containing 0.5% of conc. NH_4OH to afford 0.18 g of a crude product which was dissolved in Et_2O and treated with HCl/Et_2O to yield 0.15 g of the title compound.
$C_{27}H_{24}N_2O_3.HCl$
M.W. = 460.96
I.R. (KBr): 1745; 1640; 1610 cm^{-1}.
MS (EI; source 200 °C;70 eV; 200 μA): 424 (M+.); 365; 232; 204.

EXAMPLE 95

(R,S)-N-[α-(Methylcarbonyl)benzyl]-2-phenylquinoline-4-carboxamide

[0072] 0.27 ml (3.1 mmol) of oxalyl chloride were dissolved, under nitrogen athmosphere, in 2.3 ml of dry CH_2Cl_2. The solution was cooled to -55 °C and 0.22 ml (3.1 mmol) of DMSO, dissolved in 0.7 ml of dry CH_2Cl_2, were added dropwise maintaining the temperature below -50 °C. The reaction was stirred at -55°C for 7 minutes then 0.97 g (2.5 mmol) of (R,S)-N-[α-(1-hydroxyethyl)benzyl]-2-phenylquinoline-4-carboxamide (compound of Ex. 17), dissolved in 25 ml of dry CH_2Cl_2, were added keeping the temperature between -50 and -55 °C.
After 30 minutes at -55 °C, 1.9 ml (13.6 mmol) of TEA were added without exceeding -40 °C, then the reaction mixture was allowed to reach room temperature and stirred for additional 15 minutes.
The reaction was quenched with 5 ml of H_2O and extracted with CH_2Cl_2; the organic layer was washed with H_2O, 20% citric acid, saturated solution of $NaHCO_3$ and brine; the organic layer was separated, dried over Na_2SO_4 and evaporated *in vacuo* to dryness.
The residual oil was flash chromatographed on 230-400 mesh silica gel, eluting with a mixture of hexane/ethyl acetate 70 : 30 containing 0.5% of conc. NH_4OH to afford 0.64 g of a crude product which was triturated with warm *i*-Pr_2O/*i*-PrOH 2 : 1, filtered, washed and dried to yield 0.5 g of the title compound.
$C_{25}H_{20}N_2O_2$
M.P. = 160-161 °C
M.W. = 380.45

Elemental analysis	Calcd.	C, 78.93;	H, 5.30;	N, 7.36;
	Found	C, 79.01;	H, 5.31;	N, 7.27.

I.R. (KBr): 3400; 3265; 1725; 1660; 1640; 1592 cm^{-1}.

300 MHz 1H-NMR (DMSO-d6): 9.60 (d, 1H); 8.29 (d, 2H); 8.17 (d, 1H); 8.14 (d, 1H); 8.12 (s, 1H); 7.82 (dd, 1H); 7.65 (dd, 1H); 7.61-7.51 (m, 5H); 7.48-7.36 (m, 3H); 2.19 (s, 3H).

MS (EI; source 200 °C;70 eV; 200 μA): 380 (M+.); 337; 232; 204.

EXAMPLE 96

(R,S)-N-[α-(2-Hydroxyethyl)benzyl]-2-phenylquinoline-4-carboxamide

[0073] 0.7 g (1.7 mmol) of (R,S)-N-[α-(methoxycarbonylmethyl)benzyl]-2-phenylquinoline-4-carboxamide (com-

pound of Ex. 15) were dissolved, under nitrogen athmosphere, in 50 ml of *t*-BuOH and 2 ml of MeOH.
60 mg (1.6 mmol) of $NaBH_4$ were added in 15 minutes to the boiling solution. The reaction mixture was refluxed for 6 hours, quenched with 5 ml of saturated solution of NH_4Cl and then evaporated *in vacuo* to dryness. The residue was dissolved in CH_2Cl_2 and washed with brine; the organic layer was separated, dried over Na_2SO_4 and evaporated *in vacuo* to dryness.
The crude product was flash chromatographed on 230-400 mesh silica gel, eluting with Et_2O containing 0.5% of conc. NH_4OH and then crystallized from *i*-PrOH to yield 0.19 g of the title compound.
$C_{25}H_{22}N_2O_2$
M.P. = 167-169 °C
M.W. = 382.47

Elemental analysis	Calcd.	C, 78.52;	H, 5.80;	N, 7.32;
	Found	C, 78.49;	H, 5.79;	N, 7.29.

I.R. (KBr): 3360; 1650; 1592 cm^{-1}.

300 MHz 1H-NMR (DMSO-d6): 9.30 (d, 1H); 8.31 (d, 2H); 8.13 (d, 1H); 8.10 (s, 1H); 8.03 (d, 1H); 7.81 (dd, 1H); 7.64-7.51 (m, 4H); 7.46 (d, 2H); 7.39 (dd, 2H); 7.29 (dd, 1H); 5.30 (dt, 1H); 4.61 (t, 1H); 3.61-3.41 (m, 2H); 2.11-1.86 (m, 2H).

MS (EI; source 200 °C;70 eV; 200 μA): 382 (M+.); 337; 232; 204.

EXAMPLE 97

(S)-N-(α-Ethylbenzyl)-3-(2-dimethylaminoethoxy)-2-phenylquinoline-4-carboxamide hydrochloride

[0074] 0.62 g (1.6 mmol) of (S)-N-(α-ethylbenzyl)-3-hydroxy-2-phenylquinoline-4-carboxamide (compound of Ex. 85) were dissolved in 30 ml of dry DMF.
0.58 g (4.0 mmol) of dimethylaminoethylchloride hydrochloride and 0.56 g (4.0 mmol) of K_2CO_3 were added and the reaction mixture was refluxed for 20 hours. The K_2CO_3 was filtered off and the mixture was evaporated *in vacuo* to dryness, dissolved in AcOEt and washed with H_2O and with 20% citric acid. The aqueous layer was made alkaline with 2 N NaOH and extracted with EtOAc; the organic layer was washed with brine, separated, dried over Na_2SO_4 and evaporated *in vacuo* to dryness.
The residue was flash chromatographed on 230-400 mesh silica gel, eluting with CH_2Cl_2/MeOH 98 : 2 containing 0.4% of conc. NH_4OH and then with CH_2Cl_2/MeOH 86 : 10 containing 0.6% of conc. NH_4OH to yield 85 mg of a crude product which was dissolved in EtOAc and treated with HCl/Et_2O to obtain 75 mg of the title compound.
$C_{29}H_{31}N_3O_2$.HCl
M.P. = 70 °C dec.
M.W. = 490.05
I.R. (nujol): 3600; 3100; 1650; 1550 cm^{-1}.

300 MHz 1H-NMR (DMSO-d6): 10.28 (s br, 1H); 9.50 (d, 1H); 8.10 (d, 1H); 7.96 (dd, 2H); 7.78 (m, 1H); 7.67-7.61 (m, 2H); 7.61-7.51 (m, 3H); 7.49-7.39 (m, 4H); 7.33 (dd, 1H); 5.08 (dt, 1H); 3.90 (t, 2H); 2.96 (dt, 2H); 2.49 (s, 6H); 1.85 (m, 2H); 0.97 (t, 3H).

MS (FAB POS, thioglycerol matrix, Xe gas, 8 KeV, source 50 °C): 454 (MH+)

EXAMPLE 98

(S)-N-(α-Ethylbenzyl)-3-acetylamino-2-phenylquinoline-4-carboxamide

[0075] 0.40 g (1.05 mmol) of (S)-N-(α-ethylbenzyl)-3-amino-2-phenylquinoline-4-carboxamide (compound of Ex. 69) were heated in 25 ml of acetic anhydride at 70 °C for 1 hour and then at 100 °C for additional 3 hours.
The reaction mixture was then evaporated *in vacuo* to dryness and the residue dissolved in EtOAc; the solution was washed with water, saturated solution of $NaHCO_3$, brine, dried over Na_2SO_4 and evaporated *in vacuo* to dryness.
The crude product (0.39 g) was purified by silica gel flash column chromatography, eluting with a mixture of hexane/EtOAc/conc. NH_4OH, 70 : 30 : 0.5, respectively, to afford 0.2 g of a pure compound which was recrystallized from

acetone to yield 0.14 g of the title compound.
$C_{27}H_{25}N_3O_2$
M.P. = 268-269 °C
M. W. = 423.52

Elemental analysis	Calcd.	C, 76.57;	H, 5.95;	N, 9.92;
	Found	C, 76.38;	H, 5.98;	N, 9.90.

I.R. (KBr): 3230; 1670; 1640; 1555; 1525 cm^{-1}.

300 MHz 1H-NMR (DMSO-d6): 9.65 (s, 1H); 9.05 (d, 1H); 8.10 (d, 1H); 7.80 (t, 1H); 7.70-7.50 (m, 4H); 7.45-7.20 (m, 8H); 5.08 (dt, 1H); 1.85 (m, 2H); 1.60 (s, 3H); 0.97 (t, 3H).

MS (EI; source 200 °C;70 eV; 200 μA): 423 (M+.); 381; 334; 289; 261; 247; 218.

EXAMPLE 99

(-)-(S)-N-(α-Ethylbenzyl)-3-(3-dimethylaminopropoxy)-2-phenylquinoline-4-carboxamide hydrochloride

[0076] 1.2 g (3.1 mmol) of (-)-(S)-N-(α-ethylbenzyl)-3-hydroxy-2-phenylquinoline-4-carboxamide (compound of Ex. 85) were dissolved in 15 ml of dry THF.
1.0 g (8.2 mmol) of 3-dimethylaminopropylchloride, dissolved in 10 ml of Et_2O, 1.3 g (9.4 mmol) of K_2CO_3 and 0.16 g of KI were added and the reaction mixture was stirred at room temperature for 30 minutes and then refluxed for 2 hours. Further 0.77 g (6.3 mmol), 1.0 g (8.2 mmol), 0.6 g (4.9 mmol) and additional 0.6 g (4.9 mmol) of 3-dimethylaminopropylchloride, dissolved each time in 10 ml of Et_2O, and some KI were added every 12 hours and the reaction refluxed. The K_2CO_3 was filtered off and the mixture was evaporated *in-vacuo* to dryness, dissolved in EtOAc and washed with H_2O and with 20% citric acid. The aqueous layer was made alkaline with 2 N NaOH and extracted with EtOAc; the organic layer was washed with brine, separated, dried over Na_2SO_4 and evaporated *in-vacuo* to dryness.
The residue was flash chromatographed on 230-400 mesh silica gel, eluting with CH_2Cl_2/MeOH 95: 5 containing 0.5% of conc. NH_4OH to yield 0.9 g of a crude product which was dissolved in EtOAc and treated with HCl/Et_2O to obtain 0.62 g of the title compound.
$C_{30}H_{33}N_3O_2$.HCl
M.P. = 108°C dec.
M.W. = 504.08
$[\alpha]_D^{20}$= - 16.0 (c = 0.5, MeOH)
I.R. (KBr): 3400; 3080; 1655; 1545 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 10.55 (s br, 1H); 9.35 (d, 1H); 8.09 (d, 1H); 7.92 (dd, 2H); 7.76 (ddd, 1H); 7.65-7.51 (m, 5H); 7.48-7.40 (m, 4H); 7.31 (dd, 1H); 5.10 (dt, 1H); 3.72-3.62 (m, 2H); 2.75-2.60 (m, 2H); 2.58 (d, 3H); 2.56 (d, 3H); 1.90-1.67 (m, 4H); 1.00 (t, 3H).

MS (EI; source 180 °C; 70 V; 200 mA): 467 (M+.); 466; 395; 58.

EXAMPLE 100

(-)-(S)-N-(α-Ethylbenzyl)-3-[2-(1-phthaloyl)ethoxy]-2-phenylquinoline-4-carboxamide hydrochloride

[0077] 1.9 g (5.0 mmol) of (-)-(S)-N-(α-ethylbenzyl)-3-hydroxy-2-phenylquinoline-4-carboxamide (compound of Ex. 85) were dissolved in 20 ml of dry THF.
3.8 g (14.9 mmol) of 2-phthalimidoethylbromide, dissolved in 15 ml of THF, 2.0 g (14.5 mmol) of K_2CO_3 and 0.25 g of KI were added and the reaction mixture was stirred at room temperature for 2.5 hours and then refluxed for 2 hours. 1.9 g (7.4 mmol) of 2-phthalimidoethylbromide and some KI were added and the reaction was refluxed for additional 3.5 hours.
0.5 g (2.0 mmol) of 2-phthalimidoethylbromide and some KI were added again and the mixture was refluxed for 5 hours. The K_2CO_3 was filtered off and the mixture was evaporated *in-vacuo* to dryness, dissolved in CH_2Cl_2 and washed with H_2O. The organic layer was dried over Na_2SO_4 and evaporated *in-vacuo* to dryness.
The residue was flash chromatographed on 230-400 mesh silica gel, eluting with hexane/EtOAc 80 : 20 containing

0.5% of conc. NH_4OH and then hexane/EtOAc 60 : 40 containing 0.5% of conc. NH_4OH to afford 2.6 g of a purified product which was triturated with iPr_2O to yield 2.5 g of the title compound.
$C_{35}H_{29}N_3O_4$
M.P. = 172-175°C
M.W. = 555.64
$[\alpha]_D^{20}$= - 16.3 (c = 0.5, MeOH)
I.R. (KBr): 3280; 3060; 2960; 1780; 1715; 1660; 1530 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 9.27 (d, 1H); 8.03 (d, 1H); 7.92-7.84 (m, 4H); 7.78-7.69 (m, 3H); 7.60-7.53 (m, 2H); 7.46-7.38 (m, 4H); 7.27 (dd, 1H); 7.13-7.04 (m, 3H); 4.96 (dt, 1H); 3.92-3.78 (m, 2H); 3.72-3.55 (m, 2H); 1.78 (dq, 2H); 0.93 (t, 3H).

MS (EI; source 180 °C; 70 V; 200 mA): 555 (M+.), 526, 421, 174.

EXAMPLE 101

(-)-(S)-N-(α-Ethylbenzyl)-3-(2-aminoethoxy)-2-phenylquinoline-4-carboxamide hydrochloride

[0078] 2.2 g (3.9 mmol) of (-)-(S)-N-(α-ethylbenzyl)-3-[2-(1-phthaloyl)ethoxy]-2-phenyl quinoline-4-carboxamide hydrochloride (compound of Ex. 101) were dissolved in 150 ml of 96% EtOH and 0.38 ml (7.8 mmol) of hydrazine hydrate were added to the boiling solution, which was then refluxed for 4 hours.
Further 0.4 ml (8.2 mmol), 0.2 ml (4.1 mmol), 0.2 ml (4.1 mmol), 0.4 ml (8.2 mmol) and 0.4 ml (8.2 mmol) of hydrazine hydrate were added every 12 hours and the reaction mixture was maintained refluxed.
The reaction mixture was then evaporated *in-vacuo* to dryness, dissolved in 20 ml H_2O, cooled and acidified with 10 ml conc. HCl.
The mixture was boiled for 1 hour and cooled; the phthalydrazide was filtered off.
The aqueous layer was washed with EtOAc and then made alkaline with 2 N NaOH and extracted with EtOAc; the organic layer was washed with brine, separated, dried over Na_2SO_4 and evaporated *in-vacuo* to dryness.
The residue was flash chromatographed on 230-400 mesh silica gel, eluting with EtOAc/MeOH 96: 4 containing 1.2% of conc. NH_4OH to afford a purified product which was dissolved in EtOAc and treated with HCl/Et_2O to yield 1.2 g of the title compound.
$C_{27}H_{27}N_3O_2$.HCl
M.P. = 119°C dec.
M.W. = 462.00
$[\alpha]_D^{20}$ = - 19.4 (c = 0.5, MeOH)
I.R. (KBr): 3400; 3080; 1640; 1545 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 9.45 (d, 1H); 8.09 (d, 1H); 8.00 (dd, 1H); 7.94 (s br, 3H); 7.76 (ddd, 1H); 7.65-7.51 (m, 4H); 7.48-7.40 (m, 3H); 7.31 (dd, 1H); 5.09 (dt, 1H); 3.83 (t, 2H); 2.72 (m, 2H); 1.93-1.80 (m, 2H); 0.99 (t, 3H).

MS (FAB POS, thioglycerol matrix; Xe gas, 8 keV; source 50 °C): 426 (MH+).

EXAMPLE 102

(+)-(S)-N-(α-Ethylbenzyl)-3-[2-(1-pyrrolidinyl)ethoxy]-2-phenylquinoline-4-carboxamide hydrochloride

[0079] 2.0 g (5.2 mmol) of (-)-(S)-N-(α-ethylbenzyl)-3-hydroxy-2-phenylquinoline-4-carboxamide (compound of Ex. 85) were dissolved in 25 ml of dry THF.
1.0 g (7.5 mmol) of 2-pyrrolidinoethylchloride and 2.2 g (15.9 mmol) of K_2CO_3 were added and the reaction mixture was stirred at room temperature for 30 minutes and then refluxed; 1.1 g (8.2 mmol) of 2-pyrrolidinoethylchloride were added to the boiling solution which was refluxed overnight.
The K_2CO_3 was filtered off and the mixture was evaporated *in-vacuo* to dryness, dissolved in EtOAc and washed with H_2O and 20% citric acid. The aqueous layer was made alkaline with 2 N NaOH and extracted with EtOAc; the organic layer was washed with brine, separated, dried over Na_2SO_4 and evaporated *in-vacuo* to dryness.
The residue was flash chromatographed on 230-400 mesh silica gel, eluting with CH_2Cl_2/MeOH 97: 3 containing 0.5% of conc. NH_4OH to yield 1.8 g of a purified product which was dissolved in EtOAc and treated with HCl/Et_2O to yield 2.0 g of the title compound.

$C_{31}H_{33}N_3O_2.HCl$
M.P. = 110-115 °C (dec.)
M.W. = 516.08
$[\alpha]_D^{20}$= + 4.5 (c = 0.5, MeOH)
I.R. (KBr): 3400; 3080; 1655; 1545 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 10.50 (s br, 1H); 9.50 (d, 1H); 8.10 (d, 1H); 7.96 (dd, 2H); 7.78 (ddd, 1H); 7.68-7.30 (m, 10H); 5.10 (dt, 1H); 3.90 (m, 2H); 3.20 (m, 2H); 3.00 (m, 2H); 2.65 (m, 2H); 1.95-1.65 (m, 6H); 1.94 (t, 3H).

MS (EI; source 180 °C; 70 V; 200 mA): 479 (M+.); 478; 383; 97; 84.

EXAMPLE 103

(-)-(S)-N-(α-Ethylbenzyl)-3-(dimethylaminoacetylamino)-2-phenylquinoline-4-carboxamide

[0080] 1.1 g (2.8 mmol) of (-)-(S)-N-(α-ethylbenzyl)-3-amino-2-phenylquinoline-4-carboxamide (compound of Ex. 69) were dissolved, under nitrogen atmosphere, in 10 ml of warm toluene. 0.96 g (5.6 mmol) of chloroacetic anhydride, dissolved in 5 ml of toluene, were dropped and the solution was refluxed for 1 hour.
The reaction mixture was evaporated *in-vacuo* to dryness, suspended in 10 ml of CH_2Cl_2 and dropped in 5 ml of ice-cooled 28% Me_2NH/EtOH.
The solution was stirred at room temperature overnight, then 15 ml of 28% Me_2NH/EtOH were added and the reaction mixture was heated at 60 °C in a parr apparatus.
The mixture was evaporated *in-vacuo* to dryness, dissolved in 20% citric acid and washed with EtOAc. The aqueous layer was basified with 2 N NaOH and extracted with EtOAc; the organic layer was washed with brine, separated, dried over Na_2SO_4 and evaporated *in-vacuo* to dryness to afford 1.4 g of the crude product.
This product was triturated with warm *i*-Pr_2O to yield 0.86 g of the title compound.
$C_{29}H_{30}N_4O_2$
M.P. = 189-191 °C
M.W. = 466.59
$[\alpha]_D^{20}$= - 63.1 (c = 0.5, MeOH)
I.R. (KBr): 3230; 3180; 1670; 1630; 1540 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 9.41 (s, 1H); 8.97 (d, 1H), 8.08 (d, 1H); 7.81 (dd, 1H); 7.70-7.59 (m, 4H); 7.49-7.26 (m, 8H); 5.00 (dt, 1H); 2.55 (s, 2H); 1.97 (s, 3H); 1.90-1.65 (m, 2H); 0.93 (t, 3H).

MS (EI; source 180 °C; 70 V; 200 mA): 466 (M+.); 331; 58.

EXAMPLE 104

N-(α,α-Dimethylbenzyl)-3-hydroxy-2-phenylquinoline-4-carboxamide

[0081] 2.0 g (7.5 mmol) of 3-hydroxy-2-phenylquinoline-4-carboxylic acid were dissolved, under nitrogen atmosphere, in 70 ml of dry THF and 30 ml of CH_3CN.
1.02 g (7.5 mmol) of cumylamine and 1.12 g (8.3 mmol) of N-hydroxybenzotriazole (HOBT) were added and the reaction mixture was cooled at -10°C.
1.71 g (8.3 mmol) of DCC, dissolved in 20 ml of CH_2Cl_2, were added dropwise and the solution was kept at -5°- 0°C for 2 hours and then at room temperature overnight. The precipitated dicyclohexylurea was filtered off and the solution evaporated *in-vacuo* to dryness. The residue was dissolved in CH_2Cl_2 and washed with H_2O, sat. sol. $NaHCO_3$, 5% citric acid, sat. sol. $NaHCO_3$ and brine.
The organic layer was separated, dried over Na_2SO_4 and evaporated *in-vacuo* to dryness; the residue was dissolved in 20 ml of CH_2Cl_2 and left overnight. Some more dicyclohexylurea precipitated and was filtered off.
The solution was evaporated *in-vacuo* to dryness to obtain 1.4 g of a crude product which was flash chromatographed on 230-400 mesh silica gel, eluting initially with hexane/EtOAc 9/1 and then hexane/EtOAc 8/2 to afford 0.4 g of the purified product which was recrystallized twice from *i*-PrOH to yield 0.15 g of the title compound.
$C_{25}H_{22}N_2O_2$
M.P. = 166-169°C dec.
M.W. = 382.47

I.R. (nujol): 3200; 1650; 1580; 1535 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 9.56 (s, 1H); 8.92 (s br, 1H); 8.00-7.94 (m, 3H); 7.76 (d br, 1H); 7.63-7.45 (m, 7H); 7.36 (dd; 2H); 7:24 (dd, 1H); 1.72 (s, 6H).

MS (EI; source 180 °C; 70 V; 200 mA): 382 (M+.); 264; 247; 219; 119.

EXAMPLE 105

N-(α,α-Dimethylbenzyl)-3-amino-2-phenylquinoline-4-carboxamide

[0082] 2.0 g (7.6 mmol) of 3-amino-2-phenylquinoline-4-carboxylic acid were dissolved, under nitrogen atmosphere, in 70 ml of dry THF and 30 ml of CH_3CN.
1.02 g (7.6 mmol) of cumylamine and 1.12 g (8.3 mmol) of N-hydroxybenzotriazole (HOBT) were added and the reaction mixture was cooled at -10°C.
1.72 g (8.3 mmol) of DCC, dissolved in 20 ml of CH_2Cl_2, were added dropwise and the solution was kept at -5°- 0°C for 2 hours and then at room temperature overnight. The precipitated dicyclohexylurea was filtered off and the solution evaporated *in-vacuo* to dryness. The residue was dissolved in CH_2Cl_2 and washed with H_2O, sat. sol. $NaHCO_3$, 5% citric acid, sat. sol. $NaHCO_3$ and brine.
The organic layer was separated, dried over Na_2SO_4 and evaporated *in-vacuo* to dryness; the residue was dissolved in 20 ml of CH_2Cl_2 and left overnight. Some more dicyclohexylurea precipitated and was filtered off.
The solution was evaporated *in-vacuo* to dryness to obtain 2.0 g of a crude product which was flash chromatographed on 230-400 mesh silica gel, eluting with hexane/EtOAc 6/4 containing 1% of conc. NH_4OH to afford 0.9 g of the purified product which was recrystallized from hexane/EtOAc 1/1 and then from *i*-PrOH to yield 0.45 g of the title compound.
$C_{25}H_{23}N_3O$
M.P. = 166-168°C
M.W. = 381.48
I.R. (nujol): 3460; 3360; 3220; 1667; 1605; 1527 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 9.05 (s, 1H); 7.87 (dd, 1H); 7.74-7.68 (m, 3H); 7.60-7.42 (m, 7H); 7.37 (dd, 2H); 7.24 (dd, 1H); 4.74 (s, 2H); 1.71 (s,6H).

MS (EI; source 180 °C; 70 V; 200 mA): 381 (M+.); 263; 218; 119.

EXAMPLE 106

(-)-(S)-N-(α-Ethylbenzyl)-5-methyl-2-phenylquinoline-4-carboxamide

[0083] 0.80 g (3.04 mmol) of 5-methyl-2-phenylquinoline-4-carboxylic acid were dissolved, under nitrogen atmosphere, in 30 ml of dry THF and 12 ml of CH_3CN.
0.43 g (3.20 mmol) of (S)-(-)-α-ethylbenzylamine and 0.78 g (5.78 mmol) of N-hydroxybenzotriazole (HOBT) were added and the reaction mixture was cooled at -10°C.
0.69 g (3.34 mmol) of DCC, dissolved in 5 ml of CH_2Cl_2, were added dropwise and the solution was kept at -5°- 0°C for 2 hours and then at room temperature overnight. The precipitated dicyclohexylurea was filtered off and the solution evaporated *in-vacuo* to dryness. The residue was dissolved in CH_2Cl_2 and washed with H_2O, sat. sol. $NaHCO_3$, 5% citric acid, sat. sol. $NaHCO_3$ and brine.
The organic layer was separated, dried over Na_2SO_4 and evaporated *in-vacuo* to dryness; the residue was dissolved in 10 ml of CH_2Cl_2 and left overnight. Some more dicyclohexylurea precipitated and was filtered off.
The solution was evaporated *in-vacuo* to dryness to obtain 1.15 g of a crude product which was flash chromatographed on 230-400 mesh silica gel, eluting with hexane/EtOAc 6/2 containing 0.5% of conc. NH_4OH to afford 0.47 g of the purified product which was recrystallized from *i*-Pr_2O containing some drops of EtOAc to yield 0.36 g of the title compound as a white powder.
$C_{26}H_{24}N_2O$
M.P. = 189-192 °C
M.W. = 380.49
$[\alpha]_D^{20}$= - 3.8 (c = 0.5, MeOH)
I.R. (KBr): 3280; 3070; 3020; 1635; 1545 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 9.20 (d, 1H); 8.23 (d, 2H); 7.93 (d, 1H); 7.78 (s, 1H); 7.20-7.70 (m, 10H); 5.00 (dt, 1H); 2.38 (s broad, 3H); 1.70-1.90 (m, 2H); 0.95 (t, 3H).

MS (EI; source 180 °C; 70 V; 200 mA): 380 (M+.); 246; 218.

EXAMPLE 107

(R,S)-N-[α-(1-Hydroxyethyl)benzyl]-3-methyl-2-phenylquinoline-4-carboxamide

[0084] Prepared as described in Ex. 1, starting from 11.08 g (39.33 mmol) of crude 3-methyl-2-phenylquinoline-4-carbonylchloride, 4.87 g (32.20 mmol) of 1-phenyl-2-hydroxypropylamine and 10.33 ml (74.14 mmol) of TEA in 150 ml of a 1:1 mixture of dry CH_2Cl_2 and CH_3CN.
The precipitated TEA hydrochloride was filtered off and the filtrate concentrated *in-vacuo* to dryness; the residue was dissolved in CH_2Cl_2 (100 ml) and washed with a sat. sol. of $NaHCO_3$, 20 % citric acid and brine. The organic solution was dried over Na_2SO_4 and evaporated *in-vacuo* to dryness to obtain 13.23 g of an oil, which was crystallized from *i*-PrO_2 (100 ml) containing 6 ml of *i*-PrOH to yield 9.14 g of the title compound as an off-white solid.
$C_{26}H_{24}N_2O_2$
M.P. = 163-165 °C
M.W. = 396.49
I.R. (nujol): 3400; 3260; 1635; 1580 cm^{-1}.

EXAMPLE 108

(R,S)-N-[α-(Methylcarbonyl)benzyl]-3-methyl-2-phenylquinoline-4-carboxamide

[0085] Prepared as described in Example 96, starting from 3.25 g (25.60 mmol) of oxalyl chloride, 3.88 g (49.66 mmol) of DMSO, 8.2 g (20.68 mmol) of (R,S)-N-[α-(1-hydroxyethyl)benzyl]-3-methyl-2-phenylquinoline-4-carboxamide (compound of Ex. 108) and 15.72 ml (112.76 mmol) of TEA in 230 ml of dry CH_2Cl_2.
The reaction was quenched with 40 ml of H_2O and the organic layer separated and washed with 20% citric acid, sat. sol. $NaHCO_3$ and brine. The organic solution was dried over Na_2SO_4 and evaporated *in-vacuo* to dryness to afford 9.4 g of the crude title compound as an oil. This residual oil was flash chromatographed on 230-400 mesh silica gel, eluting with a mixture of hexane/ethyl acetate 70 : 30 containing 1% of conc. NH_4OH to afford 7.7 g of the purified product which was crystallized from a mixture of EtOAc/hexane 1 : 3 respectively, to yield 6.0 g of the pure title compound.
$C_{26}H_{22}N_2O_2$
M.P. = 156-158 °C
M.W. = 394.48
I.R. (nujol): 3270; 3180; 1735; 1725; 1660; 1630; 1527; 1460 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 9.53 (d, 1H); 8.01 (d, 1H); 7.73 (dd, 1H); 7.62-7.35 (m, 12H); 5.97 (d, 1H); 2.30 (s br, 3H); 2.18 (s, 3H).

MS (EI; source 180 °C; 70 V; 200 mA): 394 (M+.); 352; 351; 246; 218; 217.

EXAMPLE 109

(R,S)-N-[α-(Ethyl)-4-pyridylmethyl]-2-phenylquinoline-4-carboxamide

[0086] 4.12 g (16.52 mmol) of 2-phenylquinoline-4-carboxylic acid were dissolved, under nitrogen atmosphere, in 40 ml of dry CH_2Cl_2 and 30 ml of THF.
1.50 g (11.01 mmol) of 1-(4-pyridyl)-*n*-propyl amine and 2.23 g (16.52 mmol) of N-hydroxybenzotriazole (HOBT) were added and the reaction mixture was cooled at 0°C.
3.41 g (16.52 mmol) of DCC, dissolved in 26 ml of dry CH_2Cl_2, were added dropwise and the solution was kept at 0°C for 2 hours and then stirred at room temperature for 36 hours. The precipitated dicyclohexylurea was filtered off and the solution evaporated *in-vacuo* to dryness. The residue was dissolved in 100 ml of CH_2Cl_2 and washed with H_2O, 10% K_2CO_3, 5% citric acid and brine.
The organic layer was separated, dried over Na_2SO_4 and evaporated *in-vacuo* to dryness; the residue was dissolved in 30 ml of CH_2Cl_2 and left overnight. Some more dicyclohexylurea precipitated and was filtered off.
The solution was evaporated *in-vacuo* to dryness to obtain 3.5 g of a crude product which was recrystallized three

times from *i*-PrOH to yield 0.91 g of the title compound.
$C_{24}H_{21}N_3O$
M.P. = 218-219 °C
M.W. = 367.45
I.R. (KBr): 3260; 3060; 1648; 1595; 1545; 1350 cm^{-1}

300 MHz ^{1}H-NMR (DMSO-d_6): δ 9.33 (d, 1H); 8.58 (d, 2H); 8.33 (dd, 2H); 8.15 (d, 1H); 8.14 (s, 1H); 8.03 (d, 1H); 7.82 (dd, 1H); 7.66-7.52 (m, 4H); 7.47 (d, 2H); 5.05 (dt, 1H); 1.85 (dq, 2H); 1.00 (t, 3H).

MS (EI; source 180 °C; 70 V; 200 mA): 367 (M+.); 338; 232; 204.

EXAMPLE 110

(R,S)-N-[α-(Ethyl)-2-thienylmethyl]-2-phenylquinoline-4-carboxamide

[0087] 1.40 g (8.00 mmol) of 1-(2-thienyl)-*n*-propyl amine hydrochloride and 2.45 ml (17.60 mmol) of TEA were dissolved, under nitrogen atmosphere, in 50 ml of dry CH_2Cl_2 and 30 ml of CH_3CN.
2.0 g (8.00 mmol) of 2-phenylquinoline-4-carboxylic acid and 1.30 g (9.60 mmol) of N-hydroxybenzotriazole (HOBT) were added.
2.48 g (12.00 mmol) of DCC, dissolved in 30 ml of dry CH_2Cl_2, were added dropwise and the solution was stirred at room temperature for 36 hours. 50 ml of 10% HCl were added and the solution stirred for aditional 2 hours. The precipitated dicyclohexylurea was filtered off and the organic layer washed with 10% citric acid and 10% K_2CO_3.
The organic layer was separated, dried over Na_2SO_4 and evaporated *in-vacuo* to dryness. The crude product was flash chromatographed on 230-400 mesh silica gel, eluting with a mixture of hexane/EtOAc/CH_2Cl_2 80 : 15 : 0.5 to afford 2.0 g of a yellow oil which was crystallized from a mixture of toluene/hexane to yield 0.9 g of the pure title compound as white crystals.
$C_{23}H_{20}N_2OS$
M.P. = 134-137 °C
M.W. = 372.49
I.R. (KBr): 3230; 3060; 1630; 1590; 1545 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6): δ 9.33 (d, 1H); 8.30 (dd, 2H); 8.15 (d, 1H); 8.13 (d, 1H); 8.08 (s, 1H); 7.84 (ddd, 1H); 7.68-7.51 (m, 4H); 7.44 (dd, 1H); 7.11 (d, 1H); 7.02 (dd, 1H); 5.33 (dt, 1H); 2.10-1.88 (m, 2H); 1.05 (t, 3H).

MS (EI; source 180 °C; 70 V; 200 mA): 372 (M+.); 343; 232; 204.

EXAMPLE 111

(+)-(S)-N-(α-Ethylbenzyl)-3-dimethylaminomethyl-2-phenylquinoline-4-carboxamide hydrochloride

[0088] 5.60 g (21.27 mmol) of 3-methyl-2-phenylquinoline-4-carboxylic acid were dissolved in 100 ml of dichloroethane.
7.60 g (42.50 mmol) of N-bromosuccinimide and 0.52 g (2.00 mmol) of dibenzoyl peroxide were added and the solution refluxed for 24 hours.
The reaction mixture was evaporated *in-vacuo* to dryness, suspended in 100 ml of 33% Me_2NH/EtOH and stirred overnight at room temperature.
The solution was evaporated *in-vacuo* to dryness, dissolved in 50 ml of 20% K_2CO_3 and evaporated again *in-vacuo* to dryness. 50 ml of water were added to the residue and the solution, acidified with 37% HCl, was evaporated *in-vacuo* to dryness.
The crude residue and 10.8 ml (77.20 mmol) of TEA were dissolved in 50 ml of CH_2Cl_2, 50 ml of THF and 100 ml of CH_3CN.
3.00 g (22.20 mmol) of (S)-(-)-α-ethylbenzylamine, 0.78 g (5.78 mmol) of N-hydroxybenzotriazole (HOBT) and 11.9 g (57.90 mmol) of DCC were added and the solution was stirred at room temperature overnight.
The precipitated dicyclohexylurea was filtered off and the organic layer evaporated *in-vacuo* to dryness.
The brown oily residue was dissolved in 100 ml of CH_2Cl_2 and the precipitate was filtered off. The filtrate was extracted three times with 40% citric acid. The acqueous layer, basified with solid K_2CO_3, was extracted with CH_2Cl_2; the organic

solution dried over Na_2SO_4 and evaporated *in-vacuo* to dryness afforded 10 g of a brown oil.
The crude product was flash chromatographed on 230-400 mesh silica gel, eluting with a mixture of *i*-Pr_2O/CH_2Cl_2 9 : 1 to afford 2.5 g of a white solid which was dissolved in toluene and left overnight.
The DCU precipitated was filtered and the solution, treated with ethanolic HCl, was evaporated *in-vacuo* to dryness. The crude product was recrystallized from a mixture of toluene/EtOH to yield 0.7 g of the pure title compound as colourless crystals.
$C_{28}H_{29}N_3O \cdot HCl$
M.P. = 164-167 °C
M.W. = 460.02
$[\alpha]_D^{20}$= + 25.3 (c = 1, MeOH)
I.R. (KBr): 3440; 3150; 3020; 2560; 2460; 1650; 1540 cm^{-1}.

300 MHz ^{1}H-NMR (DMSO-d_6, 353 K): δ 9.70 (s br, 1H); 8.10 (d, 1H); 7.85 (dd, 1H); 7.80 (s br, 1H); 7.70-7.10 (m, 12H); 5.15 (dt, 1H); 4.38-4.20 (m, 2H); 2.30 (s, 3H); 2.22 (s, 6H); 2.10-1.82 (m, 2H); 1.00 (t, 3H).

MS (EI; source 180 °C; 70 V; 200 mA): 423 (M+.), 380, 288.

EXAMPLE 113

(S)-N-(α-Ethylbenzyl)-3-methyl-7-methoxy-2-phenylquinoline-4-carboxamide

[0089] Prepared as described in Ex. 1, starting from 1.27 g (4.09 mmol) of crude 3-methyl-7-methoxy-2-phenylquinoline-4-carbonylchloride, 0.55 g (4.09 mmol) of (S)-(-)-α-ethylbenzylamine and 1.71 ml (12.27 mmol) of TEA in 24 ml of dry CH_2Cl_2 and 1 ml of DMF to help solubility. The reaction mixture was stirred 12 hours at room temperture.
After being concentrated *in-vacuo* to dryness, the residue was dissolved in CH_2Cl_2 (30 ml) and washed with 10% $NaHCO_3$, 5% citric acid and brine. The organic solution was dried over Na_2SO_4 and evaporated *in-vacuo* to dryness to obtain 1.87 g of a crude product, which was flash chromatographed on 230-400 mesh silica gel, eluting with a mixture of hexane/EtOAc 70 : 30 to afford 0.350 g of a yellow oil.
$C_{27}H_{26}N_2O_2$
M.W. = 410.51
I.R. (KBr): 3240; 2965; 2930; 1635; 1535; 1220 cm^{-1}.

EXAMPLE 113

(S)-N-(α-Ethylbenzyl)-3-amino-5-methyl-2-phenylquinoline-4-carboxamide

[0090] 0.75 g (2.64 mmol) of 3-amino-5-methyl-2-phenylquinoline-4-carboxylic acid were dissolved, under nitrogen atmosphere, in 30 ml of dry THF and 10 ml of CH_3CN.
0.38 g (2.83 mmol) of (S)-(-)-α-ethylbenzylamine and 0.69 g (5.18 mmol) of N-hydroxybenzotriazole (HOBT) were added and the reaction mixture was cooled at -10°C.
0.61 g (2.97 mmol) of DCC, dissolved in 5 ml of CH_2Cl_2, were added dropwise and the solution was kept at -5°- 0°C for 2 hours, heated at 50 °C for 4 hours and then left at room temperature overnight.
The precipitated dicyclohexylurea was filtered off and the solution evaporated *in-vacuo* to dryness. The residue was dissolved in CH_2Cl_2 and washed with H_2O, sat. sol. $NaHCO_3$, 5% citric acid, sat. sol. $NaHCO_3$ and brine.
The organic layer was separated, dried over Na_2SO_4 and evaporated *in-vacuo* to dryness; the residue was dissolved in 10 ml of CH_2Cl_2 and left overnight. Some more dicyclohexylurea precipitated and was filtered off.
The solution was evaporated *in-vacuo* to dryness to obtain 0.86 g of a crude product which was flash chromatographed on 230-400 mesh silica gel, eluting with CH_2Cl_2/MeOH/conc. NH_4OH, 90 : 10 : 0.5 respectively, to afford 0.41 g of the title compound as an oil.
$C_{26}H_{25}N_3O$
M.W. = 395.50
I.R. (KBr): 3480; 3390; 3230; 3020; 1635; 1615; 1545 cm^{-1}.

EXAMPLE 114

(S)-N-(α-Ethylbenzyl)-3-methoxy-5-methyl-2-phenylquinoline-4-carboxamide

[0091] 1.29 g (4.40 mmol) of 3-methoxy-5-methyl-2-phenylquinoline-4-carboxylic acid were dissolved, under nitrogen atmosphere, in 40 ml of dry THF and 20 ml of CH_3CN.
0.63 g (4.62 mmol) of (S)-(-)-α-ethylbenzylamine and 1.13 g (8.36 mmol) of N-hydroxybenzotriazole (HOBT) were added and the reaction mixture was cooled at -10°C.
1.0 g (4.84 mmol) of DCC, dissolved in 5 ml of CH_2Cl_2, were added dropwise and the solution was kept at -5°- 0°C for 2 hours, heated at 50 °C for 4 hours and then left at room temperature overnight.
The precipitated dicyclohexylurea was filtered off and the solution evaporated *in-vacuo* to dryness. The residue was dissolved in CH_2Cl_2 and washed with H_2O, sat. sol. $NaHCO_3$, 5% citric acid, sat. sol. $NaHCO_3$ and brine.
The organic layer was separated, dried over Na_2SO_4 and evaporated *in-vacuo* to dryness; the residue was dissolved in 20 ml of CH_2Cl_2 and left overnight. Some more dicyclohexylurea precipitated and was filtered off.
The solution was evaporated *in-vacuo* to dryness to obtain 2.45 g of a crude product which was flash chromatographed on 230-400 mesh silica gel, eluting with hexane/EtOAc 7 : 2 containing 0.5% of conc. NH_4OH, to afford 0.28 g of the title compound as an oil.
$C_{27}H_{26}N_2O_2$
M.W. = 410.52
I.R. (KBr): 3270; 3020; 1635; 1535 cm^{-1}.

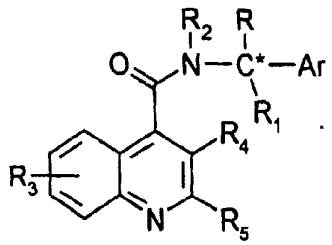
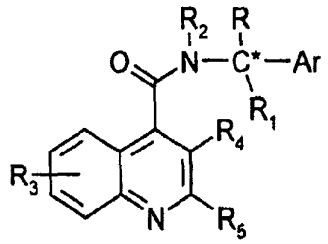


TABLE 6. Analytical data of compounds of Examples **92-114.**

Ex.	Ar	R	R_1	R_2	R_3	R_4	R_5	*	Molecular formula	Melting point, °C	$[\alpha]_D^{20}$ c=0.5 MeOH
92	Ph	COOMe	H	H	H	H	Ph(4-Cl)	(R,S)	$C_{25}H_{19}ClN_2O_3$	170-172	--
93	Ph(4-OMe)	COOMe	H	H	H	H	Ph	(R)	$C_{26}H_{22}N_2O_4$	160-162	
94	Ph	COOMe	Me	Me	H	H	Ph	(R,S)	$C_{27}H_{24}N_2O_3$. HCl		--
95	Ph	COMe	H	H	H	H	Ph	(R,S)	$C_{25}H_{20}N_2O_2$	160-161	--
96	Ph	CH_2CH_2OH	H	H	H	H	Ph	(R,S)	$C_{25}H_{22}N_2O_2$	167-169	--
97	Ph	Et	H	H	H	$OCH_2CH_2NMe_2$	Ph	(S)	$C_{29}H_{31}N_3O_2$. HCl	70 dec.[a]	--[b]
98	Ph	Et	H	H	H	NHCOMe	Ph	(S)	$C_{27}H_{25}N_3O_2$	268-269	- 71.4
99	Ph	Et	H	H	H	$OCH_2CH_2CH_2NMe_2$	Ph	(S)	$C_{30}H_{33}N_3O_2$. HCl	108 dec.	- 16.0
100	Ph	Et	H	H	H	OCH_2CH_2phthalimido	Ph	(S)	$C_{35}H_{29}N_3O_4$	172-175	- 16.3
101	Ph	Et	H	H	H	$OCH_2CH_2NH_2$	Ph	(S)	$C_{27}H_{27}N_3O_2$. HCl	119 dec.	- 19.4
102	Ph	Et	H	H	H	OCH_2CH_2pyrrolidino	Ph	(S)	$C_{31}H_{33}N_3O_2$. HCl	110-115	+ 4.5
103	Ph	Et	H	H	H	$NHCOCH_2NMe_2$	Ph	(S)	$C_{29}H_{30}N_4O_2$	189-191	- 63.1
104	Ph	Me	Me	H	H	OH	Ph	--	$C_{25}H_{22}N_2O_2$	166-169	--
105	Ph	Me	Me	H	H	NH_2	Ph	--	$C_{25}H_{23}N_3O$	166-168	--
106	Ph	Et	H	H	5-Me	H	Ph	(S)	$C_{26}H_{24}N_2O$	189-192	- 3.8

[a] free base: mp = 141-143; [b] free base: $[\alpha]_D^{20}$ = - 48.6 (c=0.5,MeOH)

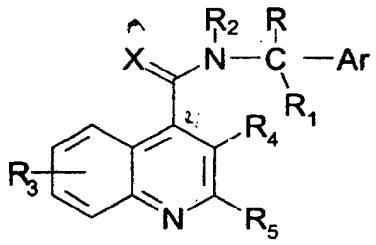
TABLE 6. (continued)



Ex.	Ar	R	R_1	R_2	R_3	R_4	R_5	*	Molecular formula	Melting point °C	$[\alpha]_D^{20}$ c=0.5M eOH
107	Ph	CH(OH)Me	H	H	H	Me	Ph	(R,S)	$C_{26}H_{24}N_2O_2$	163-165	--
108	Ph	COMe	H	H	H	Me	Ph	(R,S)	$C_{26}H_{22}N_2O_2$	156-158	--
109	4-Py	Et	H	H	H	H	Ph	(R,S)	$C_{24}H_{21}N_3O$	218-219	--
110	2-thienyl	Et	H	H	H	H	Ph	(R,S)	$C_{23}H_{20}N_2OS$	134-137	
111	Ph	Et	H	H	H	CH_2NMe_2	Ph	(S)	$C_{28}H_{29}N_3O \cdot HCl$	164-167	+ 25.3
112	Ph	Et	H	H	7-MeO	Me	Ph	(S)	$C_{27}H_{26}N_2O_2$	oil	--
113	Ph	Et	H	H	5-Me	NH2	Ph	(S)	$C_{26}H_{25}N_3O$	oil	--
114	Ph	Et	H	H	5-Me	OMe	Ph	(S)	$C_{27}H_{26}N_2O_2$	oil	--

Claims

1. A compound, or solvate or salt thereof, of formula (I):



(I)

wherein,
Ar is phenyl, 2-chlorophenyl, 2-thienyl or cyclohexadienyl;
R is methyl, ethyl, n-propyl, -COOMe, or -COMe;
R_1 and R_2 are each hydrogen or methyl;
R_3 is hydrogen, methoxy, or hydroxy;
R_4 is hydrogen, methyl, ethyl, methoxy, hydroxy, amino, chlorine, bromine, dimethylaminoethoxy, 2-(1-phthaloyl)ethoxy, aminoethoxy, 2-(1-pyrrolidinyl)ethoxy, dimethylaminopropoxy, dimethylaminoacetylamino, acetylamino, or dimethylaminomethyl;
R_5 is phenyl, 2-thienyl, 2-furyl, 2-pyrryl, 2-thiazolyl or 3-thienyl;
and X is oxygen;
with the proviso that said compound of formula (I) is not N-(α-ethylbenzyl)-3-hydroxy-2-phenylquinoline-4-carboxamide or a salt or solvate therof.

2. A compound of formula (I) as defined in claim 1, selected from the group consisting of:

(R,S)-N-(α-methylbenzyl)-2-phenylquinoline-4-carboxamide;
(+)-(S)-N-(α-methylbenzyl)-2-phenylquinoline-4-carboxamide;
(-)-(R)-N-(α-methylbenzyl)-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-phenylquinoline-4 carboxamide;
(+)-(S)-N-[α-(methoxycarbonyl)benzyl]-2-phenylquinoline-4-carboxamide;
(-)-(R)-N-[α-(methoxycarbonyl)benzyl]-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-7-methoxy-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-7-hydroxy-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(2-thienyl)quinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(2-furyl)quinoline-4-carboxamide;
(-)-(R)-N-[α-(methoxycarbonyl)-1,4-cyclohexadienylmethyl]-2-phenylquinoline-4-carboxamide;
(R,S)-N-(α-ethylbenzyl)-3-methoxy-2-phenylquinoline-4-carboxamide;
(-)-(S)-N-(α-ethylbenzyl)-3-methyl-2-phenylquinoline-4-carboxamide;
(+)-(R)-N-(α-ethylbenzyl)-3-methyl-2-phenylquinoline-4-carboxamide;
(R,S)-N-(α-ethylbenzyl)-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-3-methyl-2-phenylquinoline-4-carboxamide;
(R,S)-N-(α-ethylbenzyl)-3-methyl-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-3-ethyl-2-phenylquinoline-4-carboxamide;
(R,S)-N-(α-n-propylbenzyl)-2-phenylquinoline-4-carboxamide;
(R,S)-N-(α-ethylbenzyl)-3-ethyl-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-6-methoxy-2-phenylquinoline-4-carboxamide;
(-)-(S)-N-(α-ethylbenzyl)-3-methoxy-2-phenylquinoline-4-carboxamide;
(-)-(S)-N-(α-ethylbenzyl)-3-ethyl-2-phenylquinoline-4-carboxamide;
(R,S)-N-(α-(ethyl)-4-chlorobenzyl]-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-N-methyl-2-phenylquinoline-4-carboxamide;

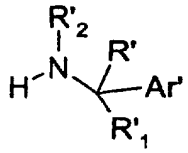
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(3-thienyl)quinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(2-pyrryl)quinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(2-thiazolyl)quinoline-4-carboxamide;
(-)-(S)-N-(α-ethylbenzyl)-3-amino-2-phenylquinoline-4-carboxamide;
(-)-(S)-N-(α-ethylbenzyl)-3-chloro-2-phenylquinoline-4-carboxamide;
(-)-(S)-N-(α-ethylbenzyl)-3-bromo-2-phenylquinoline-4-carboxamide;
(-)-(S)-N-(α-ethylbenzyl)-2-phenylquinoline-4-carboxamide;
(+)-(R)-N-(α-ethylbenzyl)-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-8-hydroxy-2-phenylquinoline-4-carboxamide;
(-)-(R)-N-[α-(methoxycarbonyl)benzyl]-3-hydroxy-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methylcarbonyl)benzyl]-2-phenylquinoline-4-carboxamide;
(-)-(S)-N-(α-ethylbenzyl)-3-(2-dimethylaminoethoxy)-2-phenylquinoline-4-carboxamide hydrochloride;
(-)-(S)-N-(α-ethylbenzyl)-3-acetylamino-2-phenylquinoline-4-carboxamide;
(-)-(S)-N-(α-ethylbenzyl)-3-(3-dimethylaminopropoxy)-2-phenylquinoline-4-carboxamide hydrochloride;
(-)-(S)-N-(α-ethylbenzyl)-3-[2-(1-phthaloyl)ethoxy]-2-phenylquinoline-4-carboxamide hydrochloride;
(-)-(S)-N-(α-ethylbenzyl)-3-(2-aminoethoxy)-2-phenylquinoline-4-carboxamide hydrochloride;
(+)-(S)-N-(α-ethylbenzyl)-3-[2-(1-pyrrolidinyl)ethoxy]-2-phenylquinoline-4-carboxamide hydrochloride;
(-)-(S)-N-(α-ethylbenzyl)-3-(dimethylaminoacetylamino)-2-phenylquinoline-4-carboxamide;
N-(α,α-dimethylbenzyl)-3-hydroxy-2-phenylquinoline-4-carboxamide;
N-(α,α-dimethylbenzyl)-3-amino-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methylcarbonyl)benzyl]-3-methyl-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(ethyl)-2-thienylmethyl]-2-phenylquinoline-4-carboxamide;
(+)-(S)-N-(α-ethylbenzyl)-3-dimethylaminomethyl-2-phenylquinoline-4-carboxamide hydrochloride; and
(S)-N-(α-ethylbenzyl)-3-methyl-7-methoxy-2-phenylquinoline-4-carboxamide.

3. An NK_3 receptor antagonist selected from the group consisting of:

(R,S)-N-[α-(carboxy)benzyl]-7-methoxy-2-phenylquinoline-4-carboxamide hydrochloride;
(R,S)-N-[α-(methylaminocarbonyl)benzyl]-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(4-pyridyl)quinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)-2-thienylmethyl]-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonylmethyl)benzyl]-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(1-hydroxyethyl)benzyl]-2-phenylquinoline-4-carboxamide single diast;
(R,S)-N-(α-ethylbenzyl)-3-n-butyl-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]benzo-1,3-cycloheptadieno[1,2-b]quinoline-8-carboxamide;
(R,S)-N-(α-ethylbenzyl)-3-hexyl-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(2-methoxyphenyl)quinoline-4-carboxamide;
(R,S)-N-(α-ethylbenzyl)-3-phenyl-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(2-fluorophenyl)quinoline-4-carboxamide;
(R,S)-N-[α-(ethyl)-3,4-dichlorobenzyl]-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(hydroxymethyl)benzyl]-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-7-chloro-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-6-methyl-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxymethyl)benzyl]-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-6-chloro-2-phenylquinoline-4-carboxamide;
(R,S)-N-(α-ethylbenzyl)-3-ethyl-2-phenylquinoline-4-carboxamide;
(R,S)-N-(α-ethylbenzyl)-3-phthalimido-2-phenylquinoline-4-carboxamide;
(R,S)-N-(α-ethylbenzyl)-3-n-propyl-2-phenylquinoline-4-carboxamide;
(-)-(S)-N-(α-ethylbenzyl)-6-bromo-3-methyl-2-(4-bromophenyl)quinoline-4-carboxamide;
(-)-(S)-N-(α-ethylbenzyl)-6-bromo-3-methyl-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(2-benzofuryl)quinoline-4-carboxamide;
(R,S)-N-[(1,2-diphenyl)ethyl]-2-phenylquinoline-4-carboxamide;
(R,S)-N-(α-trifluoromethylbenzyl)-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-5,6-dihydrobenzo[a]acridine-7-carboxamide;
(R,S)-N-(1-indanyl)-2-phenylquinoline-4-carboxamide;
(R,S)-N-(α-n-butylbenzyl)-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(4-methylphenyl)quinoline-4-carboxamide;
(R,S)-N-(α-heptylbenzyl)-2-phenylquinoline-4-carboxamide;

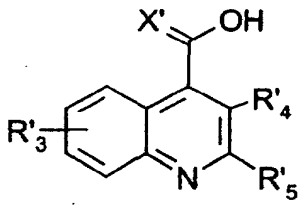
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(2-methylphenyl)quinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(4-methoxyphenyl)quinoline-4-carboxamide;
N-(1-phenylcyclopentyl)-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(4-hydroxyphenyl)quinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(3,4-methylendioxyphenyl)quinoline-4-carboxamide;
(R,S)-N-[α-(ethyl)-4-methylbenzyl]-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(3-pyrryl)quinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(3,4-dichlorophenyl)quinoline-4-carboxamide;
(-)-(R)-N-[α-(aminomethyl)benzyl]-2-phenylquinoline-4-carboxamide;
(R,S)-N-(α-*iso*-propylbenzyl)-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-6-fluoro-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-cyclohexylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(3-chlorophenyl)quinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(2-chlorophenyl)quinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-8-acetyloxy-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-8-hydroxy-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(2,4-dichlorophenyl)quinoline-4-carboxamide;
(-)-(R)-N-[α-(methoxycarbonyl)-4-hydroxybenzyl]-2-phenylquinoline-4-carboxamide hydrochloride;
N-diphenylmethyl-2-phenylquinoline-4-carboxamide;
(-)-(R)-N-[α-(dimethylaminomethyl)benzyl]-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(dimethylaminocarbonyl)benzyl]-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(aminocarbonyl)benzyl]-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(1-pyrrolidinylcarbonyl)benzyl]-2-phenylquinoline-4-carboxamide;
(-)-(R)-N-[α-(carboxy)benzyl]-2-phenylquinoline-4-carboxamide hydrochloride;
(R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(4-chlorophenyl)quinoline-4-carboxamide;
(R)-N-[α-(methoxycarbonyl)-4-methoxybenzyl)-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(methoxycarbonyl)-α-(methyl)benzyl]-N-methyl-2-phenylquinoline-4-carboxamide hydrochloride;
(R,S)-N-[α-(2-hydroxyethyl)benzyl]-2-phenylquinoline-4-carboxamide;
(-)-(S)-N-(α-ethylbenzyl)-5-methyl-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(1-hydroxyethyl)benzyl]-3-methyl-2-phenylquinoline-4-carboxamide;
(R,S)-N-[α-(ethyl)-4-pyridylmethyl]-2-phenylquinoline-4-carboxamide;
(S)-N-(α-ethylbenzyl)-3-amino-5-methyl-2-phenylquinoline-4-carboxamide; and
(S)-N-(α-ethylbenzyl)-3-methoxy-5-methyl-2-phenylquinoline-4-carboxamide.

4. A process for preparing a compound of formula (I) as defined in claim 1 or claim 2, a compound as claimed in claim 3, or a solvate or salt thereof, which comprises reacting a compound of formula (III)



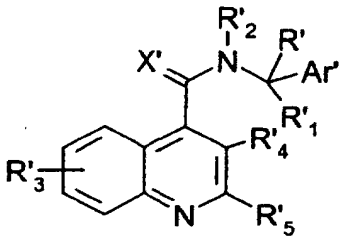
(III)

in which R', R'_1, R'_2 and Ar' are R, R_1, R_2 and Ar as defined for formula (I) or a group or atom convertible to R, R_1, R_2 and Ar, with a compound of formula (II)



(II)

or an active derivative thereof, in which R'_3, R'_4, R'_5 and X' are R_3, R_4, R_5 and X as defined for formula (I) or a group convertible to R_3, R_4, R_5 and X, to form a compound of formula (Ic)



(Ic)

and optionally thereafter performing one or more of the following steps:

(a) where R', R'_1 to R'_5, Ar' and X' are other than R, R_1 to R_5, Ar and X, converting any one of R', R'_1 to R'_5, Ar' and X' to R, R_1 to R_5, Ar and X to obtain a compound of formula (I) or a compound as defined in claim 3,
(b) where R', R'_1 to R'_5, Ar' and X' are R, R_1 to R_5, Ar and X, converting any one of R, R_1 to R_5, Ar and X to another R, R_1 to R_5, Ar and X, to obtain a compound of formula (I) or a compound as defined in claim 3,
(c) forming a salt and/or solvate of the obtained compound of formula (Ic) or a compound as defined in claim 3.

5. A process according to claim 4 in which the active derivative of the compound of formula (II) is an acid halide.

6. A pharmaceutical composition comprising a compound of formula (I) or salt or solvate thereof, as defined in claim 1 or claim 2, and a pharmaceutically acceptable carrier.

7. A pharmaceutical composition comprising a compound as defined in claim 3 or salt or solvate thereof, and a pharmaceutically acceptable carrier.

8. A compound of formula (I), or a solvate or salt thereof, as defined in claim 1 or claim 2, for use as an active therapeutic substance.

9. A compound as defined in claim 3, or a solvate or salt thereof, for use as an active therapeutic substance.

10. A compound of formula (I), or a solvate or salt thereof, as defined in claim 1 or claim 2, for use in treating pulmonary disorders (asthma, chronic obstructive pulmonary diseases -COPD-, airway hyperreactivity, cough), skin disorders and itch (for example, atopic dermatitis and cutaneous wheal and flare), neurogenic inflammation and CNS disorders (Parkinson's disease, movement disorders, anxiety and psychosis), convulsive disorders, epilepsy, renal disorders, urinary incontinence, ocular inflammation, inflammatory pain, eating disorders (food intake inhibition), allergic rhinitis, neurodegenerative disorders (for example Alzheimer's disease), psoriasis, Huntington's disease, and depression.

11. A compound as defined in claim 3, or a solvate or salt thereof, for use in treating pulmonary disorders (asthma, chronic obstructive pulmonary diseases -COPD-, airway hyperreactivity, cough), skin disorders and itch (for example, atopic dermatitis and cutaneous wheal and flare), neurogenic inflammation and CNS disorders (Parkinson's disease, movement disorders, anxiety and psychosis), convulsive disorders, epilepsy, renal disorders, urinary in-

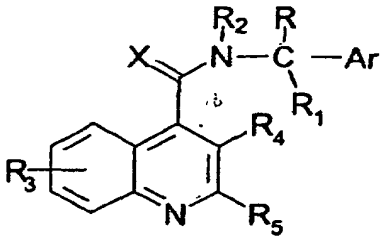
continence, ocular inflammation, inflammatory pain, eating disorders (food intake inhibition), allergic rhinitis, neurodegenerative disorders (for example Alzheimer's disease), psoriasis, Huntington's disease, and depression.

12. Use of a compound of formula (I), or a solvate or salt thereof, as defined in claim 1 or claim 2 in the manufacture of a medicament for use in the treatment of pulmonary disorders (asthma, chronic obstructive pulmonary diseases -COPD-, airway hyperreactivity, cough), skin disorders and itch (for example, atopic dermatitis and cutaneous wheal and flare), neurogenic inflammation and CNS disorders (Parkinson's disease, movement disorders, anxiety and psychosis), convulsive disorders, epilepsy, renal disorders, urinary incontinence, ocular inflammation, inflammatory pain, eating disorders (food intake inhibition), allergic rhinitis, neurodegenerative disorders (for example Alzheimer's disease), psoriasis, Huntington's disease, and depression.

13. Use of a compound as defined in claim 3, or a solvate or salt thereof, in the manufacture of a medicament for use in the treatment of pulmonary disorders (asthma, chronic obstructive pulmonary diseases -COPD-, airway hyperreactivity, cough), skin disorders and itch (for example, atopic dermatitis and cutaneous wheal and flare), neurogenic inflammation and CNS disorders (Parkinson's disease, movement disorders, anxiety and psychosis), convulsive disorders, epilepsy, renal disorders, urinary incontinence, ocular inflammation, inflammatory pain, eating disorders (food intake inhibition), allergic rhinitis, neurodegenerative disorders (for example Alzheimer's disease), psoriasis, Huntington's disease, and depression.

Patentansprüche

1. Verbindung der Formel (I) oder ein Solvat oder ein Salz davon:



(I)

wobei

Ar	Phenyl, 2-Chlorphenyl, 2-Thienyl oder Cyclohexadienyl darstellt;
R	Methyl, Ethyl, n-Propyl, -COOMe oder -COMe darstellt;
R_1 und R_2	jeweils Wasserstoff oder Methyl sind;
R_3	Wasserstoff, Methoxy oder Hydroxy ist;
R_4	Wasserstoff, Methyl, Ethyl, Methoxy, Hydroxy, Amino, Chlor, Brom, Dimethylaminoethoxy, 2-(1-Phthaloyl)ethoxy, Aminoethoxy, 2-(1-Pyrrolidinyl)ethoxy, Dimethylaminopropoxy, Dimethylaminoacetylamino, Acetylamino oder Dimethylaminomethyl ist;
R_5	Phenyl, 2-Thienyl, 2-Furyl, 2-Pyrryl, 2-Thiazolyl oder 3-Thienyl ist; und
X	Sauerstoff ist;

mit der Maßgabe, dass die Verbindung der Formel (I) nicht N-(α-Ethylbenzyl)-3-hydroxy-2-phenylchinolin-4-carboxamid oder ein Salz oder Solvat davon darstellt.

2. Verbindung der Formel (I) wie in Anspruch 1 definiert, ausgewählt aus:

(R,S)-N-(α-Methylbenzyl)-2-phenylchinolin-4-carboxamid;
(+)-(S)-N-(α-Methylbenzyl)-2-phenylchinolin-4-carboxamid;
(-)-(R)-N-(α-Methylbenzyl)-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-phenylchinolin-4-carboxamid;
(+)-(S)-N-[α-(Methoxycarbonyl)benzyl]-2-phenylchinolin-4-carboxamid;

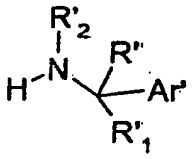
(-)-(R)-N-[α-(Methoxycarbonyl)benzyl]-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-7-methoxy-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-7-hydroxy-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(2-thienyl)chinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(2-furyl)chinolin-4-carboxamid;
(-)-(R)-N-[α-(Methoxycarbonyl)-1,4-cyclohexadienylmethyl]-2-phenylchinolin-4-carboxamid;
(R,S)-N-(α-Ethylbenzyl)-3-methoxy-2-phenylchinolin-4-carboxamid;
(-)-(S)-N-(α-Ethylbenzyl)-3-methyl-2-phenylchinolin-4-carboxamid;
(+)-(R)-N-(α-Ethylbenzyl)-3-methyl-2-phenylchinolin-4-carboxamid;
(R,S)-N-(α-Ethylbenzyl)-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-3-methyl-2-phenylchinolin-4-carboxamid;
(R,S)-N-(α-Ethylbenzyl)-3-methyl-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-3-ethyl-2-phenylchinolin-4-carboxamid;
(R,S)-N-(α-n-Propylbenzyl)-2-phenylchinolin-4-carboxamid;
(R,S)-N-(α-Ethylbenzyl)-3-ethyl-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-6-methoxy-2-phenylchinolin-4-carboxamid;
(-)-(S)-N-(α-Ethylbenzyl)-3-methoxy-2-phenylchinolin-4-carboxamid;
(-)-(S)-N-(α-Ethylbenzyl)-3-ethyl-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Ethyl)-4-chlorbenzyl]-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-N-methyl-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(3-thienyl)chinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(2-pyrryl)chinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(2-thiazolyl)chinolin-4-carboxamid;
(-)-(S)-N-(α-Ethylbenzyl)-3-amino-2-phenylchinolin-4-carboxamid;
(-)-(S)-N-(α-Ethylbenzyl)-3-chlor-2-phenylchinolin-4-carboxamid;
(-)-(S)-N-(α-Ethylbenzyl)-3-brom-2-phenylchinolin-4-carboxamid;
(-)-(S)-N-(α-Ethylbenzyl)-2-phenylchinolin-4-carboxamid;
(+)-(R)-N-(α-Ethylbenzyl)-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-8-hydroxy-2-phenylchinolin-4-carboxamid;
(-)-(R)-N-[α-(Methoxycarbonyl)benzyl]-3-hydroxy-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methylcarbonyl)benzyl]-2-phenylchinolin-4-carboxamid;
(-)-(S)-N-(α-Ethylbenzyl)-3-(2-dimethylaminoethoxy)-2-phenylchinolin-4-carboxamid-Hydrochlorid;
(-)-(S)-N-(α-Ethylbenzyl)-3-acetylamino-2-phenylchinolin-4-carboxamid;
(-)-(S)-N-(α-Ethylbenzyl)-3-(3-dimethylaminopropoxy)-2-phenylchinolin-4-carboxamid-Hydrochlorid;
(-)-(S)-N-(α-Ethylbenzyl)-3-[2-(1-phthaloyl)ethoxy]-2-phenylchinolin-4-carboxamid-Hydrochlorid;
(-)-(S)-N-(α-Ethylbenzyl)-3-(2-aminoethoxy)-2-phenylchinolin-4-carboxamid-Hydrochlorid;
(+)-(S)-N-(α-Ethylbenzyl)-3-(2-(1-pyrrolidinyl)ethoxy]-2-phenylchinolin-4-carboxamid-Hydrochlorid;
(-)-(S)-N-(α-Ethylbenzyl)-3-(dimethylaminoacetylamino)-2-phenylchinolin-4-carboxamid;
N-(α,α-Dimethylbenzyl)-3-hydroxy-2-phenylchinolin-4-carboxamid;
N-(α,α-Dimethylbenzyl)-3-amino-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methylcarbonyl)benzyl]-3-methyl-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Ethyl)-2-thienylmethyl]-2-phenylchinolin-4-carboxamid;
(+)-(S)-N-(α-Ethylbenzyl)-3-dimethylaminomethyl-2-phenylchinolin-4-carboxamid-Hydrochlorid; und
(S)-N-(α-Ethylbenzyl)-3-methyl-7-methoxy-2-phenylchinolin-4-carboxamid.

3. NK_3-Rezeptorantagonist, ausgewählt aus:

(R,S)-N-[α-(Carboxy)benzyl]-7-methoxy-2-phenylchinolin-4-carboxamid-Hydrochlorid;
(R,S)-N-[α-(Methylaminocarbonyl)benzyl]-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(4-pyridyl)chinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)-2-thienylmethyl]-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonylmethyl)benzyl]-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(1-Hydroxyethyl)benzyl]-2-phenylchinolin-4-carboxamid, einzelnes Diastereomer;
(R,S)-N-(α-Ethylbenzyl)-3-n-butyl-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]benzo-1,3-cycloheptadieno[1,2-b]chinolin-8-carboxamid;
(R,S)-N-(α-Ethylbenzyl)-3-hexyl-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(2-methoxyphenyl)chinolin-4-carboxamid;
(R,S)-N-(α-Ethylbenzyl)-3-phenyl-2-phenylchinolin-4-carboxamid;

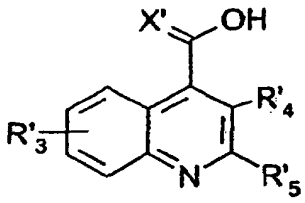
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(2-fluorphenyl)chinolin-4-carboxamid;
(R,S)-N-[α-(Ethyl)-3,4-dichlorbenzyl]-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Hydroxymethyl)benzyl]-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-7-chlor-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-6-methyl-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxymethyl)benzyl]-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-6-chlor-2-phenylchinolin-4-carboxamid;
(R,S)-N-(α-Ethylbenzyl)-3-ethyl-2-phenylchinolin-4-carboxamid;
(R,S)-N-(α-Ethylbenzyl)-3-phthalimido-2-phenylchinolin-4-carboxamid;
(R,S)-N-(α-Ethylbenzyl)-3-n-propyl-2-phenylchinolin-4-carboxamid;
(-)-(S)-N-(α-Ethylbenzyl)-6-brom-3-methyl-2-(4-bromphenyl)chinolin-4-carboxamid;
(-)-(S)-N-(α-Ethylbenzyl)-6-brom-3-methyl-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(2-benzofuryl)chinolin-4-carboxamid;
(R,S)-N-[(1,2-Diphenyl)ethyl]-2-phenylchinolin-4-carboxamid;
(R,S)-N-(α-Trifluormethylbenzyl)-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-5,6-dihydrobenzo[a]acridin-7-carboxamid;
(R,S)-N-(1-Indanyl)-2-phenylchinolin-4-carboxamid;
(R,S)-N-(α-n-Butylbenzyl)-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(4-methylphenyl)chinolin-4-carboxamid;
(R,S)-N-(α-Heptylbenzyl)-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(2-methylphenyl)chinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(4-methoxyphenyl)chinolin-4-carboxamid;
N-(1-Phenylcyclopentyl)-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(4-hydroxyphenyl)chinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(3,4-methylendioxyphenyl)chinolin-4-carboxamid;
(R,S)-N-[α-(Ethyl)-4-methylbenzyl]-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(3-pyrryl)chinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(3,4-dichlorphenyl)chinolin-4-carboxamid;
(-)-(R)-N-[α-(Aminomethyl)benzyl]-2-phenylchinolin-4-carboxamid;
(R,S)-N-(α-*iso*-Propylbenzyl)-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-6-fluor-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-cyclohexylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(3-chlorphenyl)chinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(2-chlorphenyl)chinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-8-acetyloxy-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-8-hydroxy-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(2,4-dichlorphenyl)chinolin-4-carboxamid;
(-)-(R)-N-[α-(Methoxycarbonyl)-4-hydroxybenzyl]-2-phenylchinolin-4-carboxamid-Hydrochlorid;
N-Diphenylmethyl-2-phenylchinolin-4-carboxamid;
(-)-(R)-N-[α-(Dimethylaminomethyl)benzyl]-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Dimethylaminocarbonyl)benzyl]-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Aminocarbonyl)benzyl]-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(1-pyrrolidinylcarbonyl)benzyl]-2-phenylchinolin-4-carboxamid;
(-)-(R)-N-[α-(Carboxy)benzyl]-2-phenylchinolin-4-carboxamid-Hydrochlorid;
(R,S)-N-[α-(Methoxycarbonyl)benzyl]-2-(4-chlorphenyl)chinolin-4-carboxamid;
(R)-N-[α-(Methoxycarbonyl)-4-methoxybenzyl]-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Methoxycarbonyl)-α-(methyl)benzyl]-N-methyl-2-phenylchinolin-4-carboxamid-Hydrochlorid;
(R,S)-N-[α-(2-Hydroxyethyl)benzyl]-2-phenylchinolin-4-carboxamid;
(-)-(S)-N-(α-Ethylbenzyl)-5-methyl-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(1-Hydroxyethyl)benzyl]-3-methyl-2-phenylchinolin-4-carboxamid;
(R,S)-N-[α-(Ethyl)-4-pyridylmethyl]-2-phenylchinolin-4-carboxamid;
(S)-N-(α-Ethylbenzyl)-3-amino-5-methyl-2-phenylchinolin-4-carboxamid; und
(S)-N-(α-Ethylbenzyl)-3-methoxy-5-methyl-2-phenylchinolin-4-carboxamid.

4. Verfahren zur Herstellung einer Verbindung der Formel (I) wie in Anspruch 1 oder 2 definiert, einer Verbindung nach Anspruch 3, oder eines Solvats oder Salzes davon, umfassend das Umsetzen einer Verbindung der Formel (III)



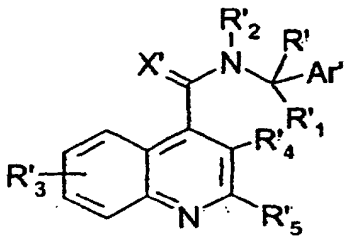
(III)

in der die Reste R', R'_1, R'_2 und Ar' die Reste R, R_1, R_2 und Ar wie für Formel (I) definiert, oder eine Gruppe oder ein Atom darstellen, die sich in R, R_1, R_2 und Ar umwandeln lässt, mit einer Verbindung der Formel (II)



(II)

oder einem aktiven Derivat davon, wobei die Reste R'_3, R'_4, R'_5 und X' die Reste R_3, R_4, R_5 und X wie für Formel (I) definiert oder eine Gruppe darstellen, die sich in R_3, R_4, R_5 und X umwandeln lässt, um eine Verbindung der Formel (Ic) zu bilden



(Ic)

und danach gegebenenfalls das Durchführen eines oder mehrerer der folgenden Schritte:

a) sofern R', R'_1 bis R'_5, Ar' und X' nicht R, R_1 bis R_5, Ar und X sind, Umwandeln jedes R', R'_1 bis R'_5, Ar' und X' in R, R_1 bis R_5, Ar und X, um eine Verbindung der Formel (I) oder eine Verbindung wie in Anspruch 3 definiert zu erhalten;
b) sofern R', R'_1 bis R'_5, Ar' und X' die Reste R, R_1 bis R_5, Ar und X sind, Umwandeln jedes R, R_1 bis R_5, Ar und X in ein weiteres R, R_1 bis R_5, Ar und X, um eine Verbindung der Formel (I) oder eine Verbindung wie in Anspruch 3 definiert zu erhalten;
c) Bilden eines Salzes und/oder eines Solvats aus der erhaltenen Verbindung der Formel (Ic) oder einer Verbindung wie in Anspruch 3 definiert.

5. Verfahren nach Anspruch 4, in dem das aktive Derivat der Verbindung der Formel (II) ein Säurehalogenid darstellt.

6. Arzneimittel, umfassend eine Verbindung der Formel (I) oder ein Salz oder Solvat davon, wie in Anspruch 1 oder 2 definiert, und einen pharmazeutisch verträglichen Träger.

7. Arzneimittel, umfassend eine Verbindung wie in Anspruch 3 definiert oder ein Salz oder Solvat davon, und ein

pharmazeutisch verträglicher Träger.

8. Verbindung der Formel (I) oder ein Solvat oder Salz davon wie in Anspruch 1 oder 2 definiert zur Verwendung als therapeutischen Wirkstoff.

9. Verbindung nach Anspruch 3, oder ein Solvat oder Salz davon, zur Verwendung als therapeutischen Wirkstoff.

10. Verbindung der Formel (I), oder ein Solvat oder Salz davon wie in Anspruch 1 oder 2 definiert zur Verwendung bei der Behandlung von Lungenerkrankungen (Asthma, chronische obstruktive Lungenerkrankungen - COPD-, Atemwegshyperreaktivität, Husten), Hauterkrankungen und Juckreiz (z.B. atopische Dermatitis und Hautquaddeln und Flare), neurogenen Entzündungen und Störungen des zentralen Nervensystems (Parkinson Krankheit, Bewegungsstörungen, Angst und Psychosen), konvulsiven Störungen, Epilepsie, Nierenerkrankungen, Harninkontinenz, Augenentzündung, entzündlichem Schmerz, Essstörung (Hemmung der Nahrungsaufnahme), allergischer Rhinitis, neurodegenerativen Erkrankungen (z.B. Alzheimer Krankheit), Psoriasis, Huntington Chorea und Depression.

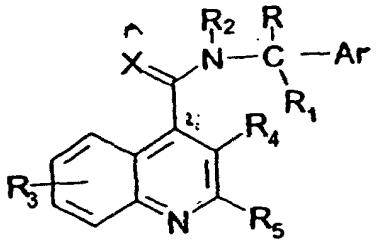
11. Verbindung wie in Anspruch 3 definiert oder ein Solvat oder Salz davon zur Verwendung bei der Behandlung von Lungenerkrankungen (Asthma, chronische obstruktive Lungenerkrankungen - COPD-, Atemwegshyperreaktivität, Husten), Hauterkrankungen und Juckreiz (z.B. atopische Dermatitis und Hautquaddeln und Flare), neurogenen Entzündungen und Störungen des zentralen Nervensystems (Parkinson Krankheit, Bewegungsstörungen, Angst und Psychosen), konvulsiven Störungen, Epilepsie, Nierenerkrankungen, Harninkontinenz, Augenentzündung, entzündlichem Schmerz, Essstörung (Hemmung der Nahrungsaufnahme), allergischer Rhinitis, neurodegenerativen Erkrankungen (z.B. Alzheimer Krankheit), Psoriasis, Huntington Chorea und Depression.

12. Verwendung einer Verbindung der Formel (I) oder eines Solvats oder Salzes davon wie in Anspruch 1 oder 2 definiert bei der Herstellung eines Medikaments zur Verwendung bei der Behandlung von Lungenerkrankungen (Asthma, chronische obstruktive Lungenerkrankungen -COPD-, Atemwegshyperreaktivität, Husten), Hauterkrankungen und Juckreiz (z.B. atopische Dermatitis und Hautquaddeln und Flare), neurogenen Entzündungen und Störungen des zentralen Nervensystems (Parkinson Krankheit, Bewegungsstörungen, Angst und Psychosen), konvulsiven Störungen, Epilepsie, Nierenerkrankungen, Harninkontinenz, Augenentzündung, entzündlichem Schmerz, Essstörung (Hemmung der Nahrungsaufnahme), allergischer Rhinitis, neurodegenerativen Erkrankungen (z.B. Alzheimer Krankheit), Psoriasis, Huntington Chorea und Depression.

13. Verwendung einer Verbindung wie in Anspruch 3 definiert oder eines Solvats oder Salzes davon bei der Herstellung eines Medikaments zur Verwendung bei der Behandlung von Lungenerkrankungen (Asthma, chronische obstruktive Lungenerkrankungen - COPD-, Atemwegshyperreaktivität, Husten), Hauterkrankungen und Juckreiz (z.B. atopische Dermatitis und Hautquaddeln und Flare), neurogenen Entzündungen und Störungen des zentralen Nervensystems (Parkinson Krankheit, Bewegungsstörungen, Angst und Psychosen), konvulsiven Störungen, Epilepsie, Nierenerkrankungen, Harninkontinenz, Augenentzündung, entzündlichem Schmerz, Essstörung (Hemmung der Nahrungsaufnahme), allergischer Rhinitis, neurodegenerativen Erkrankungen (z.B. Alzheimer Krankheit), Psoriasis, Huntington Chorea und Depression.

Revendications

1. Composé, ou un de ses produits de solvatation ou sels, de formule (I) :



(I)

dans laquelle,

Ar représente un groupe phényle, 2-chlorophényle, 2-thiényle ou cyclohexadiényle ;

R représente un groupe méthyle, éthyle, n-propyle, -COOMe ou -COMe ;

R_1 et R_2 représentent chacun un atome d'hydrogène ou un groupe méthyle ;

R_3 représente un atome d'hydrogène, un groupe méthoxy ou hydroxy ;

R_4 représente un atome d'hydrogène, un groupe méthyle, éthyle, méthoxy, hydroxy, amino, chloro, bromo, diméthylaminoéthoxy, 2-(1-phtaloyl)éthoxy, aminoéthoxy, 2-(1-pyrrolidinyl)éthoxy, diméthylaminopropoxy, diméthylaminoacétylamino, acétylamino ou diméthylaminométhyle ;

R_5 représente un groupe phényle, 2-thiényle, 2-furyle, 2-pyrryle, 2-triazolyle ou 3-thiényle ;

et X représente un atome d'oxygène ;

sous réserve que ledit composé de formule (I) ne soit pas le N-(α-éthylbenzyl)-3-hydroxy-2-phénylquinoléine-4-carboxamide ou un de ses sels ou produits de solvatation.

2. Composé de formule (I) suivant la revendication 1, choisi dans le groupe consistant en :

(R,S)-N-(α-méthylbenzyl)-2-phénylquinoléine-4-carboxamide ;
(+)-(S)-N-(α-méthylbenzyl)-2-phénylquinoléine-4-carboxamide ;
(-)-(R)-N-(α-méthylbenzyl)-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-phénylquinoléine-4-carboxamide ;
(+)-(S)-N-[α-(méthoxycarbonyl)benzyl]-2-phénylquinoléine-4-carboxamide ;
(-)-(R)-N-[α-(méthoxycarbonyl)benzyl]-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-7-méthoxy-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-7-hydroxy-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-(2-thiényl)quinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-(2-furyl)quinoléine-4-carboxamide ;
(-)-(R)-N-[α-(méthoxycarbonyl)-1,4-cyclohexadiénylméthyl]-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-(α-éthylbenzyl)-3-méthoxy-2-phénylquinoléine-4-carboxamide ;
(-)-(S)-N-(α-éthylbenzyl)-3-méthyl-2-phénylquinoléine-4-carboxamide ;
(+)-(R)-N-(α-éthylbenzyl)-3-méthyl-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-(α-éthylbenzyl)-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-3-méthyl-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-(α-éthylbenzyl)-3-méthyl-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-3-éthyl-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-(α-n-propylbenzyl)-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-(α-éthylbenzyl)-3-éthyl-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-6-méthoxy-2-phénylquinoléine-4-carboxamide ;
(-)-(S)-N-(α-éthylbenzyl)-3-méthoxy-2-phénylquinoléine-4-carboxamide ;
(-)-(S)-N-(α-éthylbenzyl)-3-éthyl-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(éthyl)-4-chlorobenzyl]-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-N-méthyl-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-(3-thiényl)quinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-(2-pyrryl)quinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-(2-thiazolyl)quinoléine-4-carboxamide ;
(-)-(S)-N-(α-éthylbenzyl)-3-amino-2-phénylquinoléine-4-carboxamide ;
(-)-(S)-N-(α-éthylbenzyl)-3-chloro-2-phénylquinoléine-4-carboxamide ;
(-)-(S)-N-(α-éthylbenzyl)-3-bromo-2-phénylquinoléine-4-carboxamide ;
(-)-(S)-N-(α-éthylbenzyl)-2-phénylquinoléine-4-carboxamide ;
(+)-(R)-N-(α-éthylbenzyl)-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-8-hydroxy-2-phénylquinoléine-4-carboxamide ;
(-)-(R)-N-[α-(méthoxycarbonyl)benzyl]-3-hydroxy-2-phénylquinoléine-4-carboxamide ;
chlorhydrate de (R,S)-N-[α-(méthylcarbonyl)benzyl]-2-phényl-quinoléine-4-carboxamide ;
chlorhydrate de (-)-(S)-N-(α-éthylbenzyl)-3-(diméthylaminoéthoxy)-2-phénylquinoléine-4-carboxamide ;
(-)-(S)-N-(α-éthylbenzyl)-3-acétylamino-2-phénylquinoléine-4-carboxamide ;
chlorhydrate de (-)-(S)-N-(α-éthylbenzyl)-3-(3-diméthylaminopropoxy)-2-phénylquinoléine-4-carboxamide ;
chlorhydrate de (-)-(S)-N-(α-éthylbenzyl)-3-[2-(1-phtaloyl)-éthoxy]-2-phénylquinoléine-4-carboxamide ;
chlorhydrate de (-)-(S)-N-(α-éthylbenzyl)-3-(2-aminoéthoxy)-2-phénylquinoléine-4-carboxamide ;
chlorhydrate de (+)-(S)-N-(α-éthylbenzyl)-3-[2-(1-pyrrolidinyl)éthoxy]-2-phénylquinoléine-4-carboxamide ;
(-)-(S)-N-(α-éthylbenzyl)-3-(diméthylaminoacétylamino)-2-phénylquinoléine-4-carboxamide ;

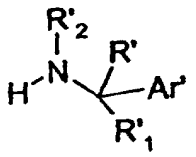
N-(α,α-diméthylbenzyl)-3-hydroxy-2-phénylquinoléine-4-carboxamide ;
N-(α,α-diméthylbenzyl)-3-amino-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthylcarbonyl)benzyl]-3-méthyl-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(éthyl)-2-thiénylméthyl]-2-phénylquinoléine-4-carboxamide ;
chlorhydrate de (+)-(S)-N-(α-éthylbenzyl)-3-diméthylaminométhyl-2-phénylquinoléine-4-carboxamide ; et
(S)-N-(α-éthylbenzyl)-3-méthyl-7-méthoxy-2-phénylquinoléine-4-carboxamide.

3. Antagoniste des récepteurs NK_3, choisi dans le groupe consistant en :

chlorhydrate de (R,S)-N-[a-(carboxy)benzyl]-7-méthoxy-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthylaminocarbonyl)benzyl]-2-phénylquinoléine-4-carboxamide ;
(R, S)-N-[α-(méthoxycarbonyl)benzyl]-2-(4-pyridyl)quinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)2-thiénylméthyl]-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonylméthyl)benzyl]-2-phénylquinoléine-4-carboxamide ;
diast. unique de (R,S)-N-[α-(1-hydroxyéthyl)benzyl]-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-(α-éthylbenzyl)-3-n-butyl-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]benzo-1,3-cycloheptadiéno-[1,2-b]quinoléine-8-carboxamide ;
(R,S)-N-(α-éthylbenzyl)-3-hexyl-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-(2-méthoxyphényl)quinoléine-4-carboxamide ;
(R,S)-N-(α-éthylbenzyl)-3-phényl-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-(2-fluorophényl)quinoléine-4-carboxamide ;
(R,S)-N-[α-(éthyl)-3,4-dichlorobenzyl]-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(hydroxyméthyl)benzyl]-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-7-chloro-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-6-méthyl-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxyméthyl)benzyl]-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-6-chloro-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-(α-éthylbenzyl)-3-éthyl-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-(α-éthylbenzyl)-3-phthalimido-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-(α-éthylbenzyl)-3-n-propyl-2-phénylquinoléine-4-carboxamide ;
(-)-(S)-N-(α-éthylbenzyl)-6-bromo-3-méthyl-2-(4-bromophényl)quinoléine-4-carboxamide ;
(-)-(S)-N-(α-éthylbenzyl)-6-bromo-3-méthyl-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-(2-benzofuryl)-quinoléine-4-carboxamide ;
(R,S)-N-[(1,2-diphényl)éthyl]-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-(α-trifluorométhylbenzyl)-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-5,6-dihydrobenzo-[a]acridine-7-carboxamide ;
(R,S)-N-(1-indanyl)-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-(α-n-butylbenzyl)-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-(4-méthylphényl)quinoléine-4-carboxamide ;
(R,S)-N-(α-heptylbenzyl)-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-(2-méthylphényl)-quinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-(4-méthoxyphényl)quinoléine-4-carboxamide ;
N-(1-phénylcyclopentyl)2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-(4-hydroxyphényl)-quinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-(3,4-méthylènedioxyphényl)quinoléine-4-carboxamide ;
(R,S)-N-[α-(éthyl)-4-méthylbenzyl]-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-(3-pyrryl)quinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-(3,4-dichlorophényl)quinoléine-4-carboxamide ;
(-)-(R)-N-[α-(aminométhyl)benzyl]-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-(α-iso-propylbenzyl)-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-6-fluoro-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-cyclohexylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-(3-chlorophényl)quinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-(2-chlorophényl)quinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-8-acétyloxy-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-8-hydroxy-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-(2,4-dichlorophényl)quinoléine-4-carboxamide ;
chlorhydrate de (-)-(R)-N-[α-(méthoxycarbonyl)-4-hydroxybenzyl]-2-phénylquinoléine-4-carboxamide ;

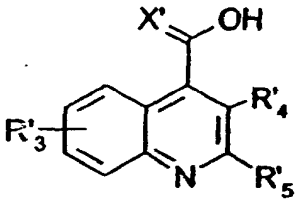
N-diphénylméthyl-2-phénylquinoléine-4-carboxamide ;
(-)-(R)-N-[α-(diméthylaminoéthyl)benzyl]-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(diméthylaminocarbonyl)benzyl]-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(aminocarbonyl)benzyl]-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(1-pyrrolidinylcarbonyl)benzyl]-2-phénylquinoléine-4-carboxamide ;
chlorhydrate de (-)-(R)-N-[α-(carboxy)benzyl]-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(méthoxycarbonyl)benzyl]-2-(4-chlorophényl)quinoléine-4-carboxamide ;
(R)-N-[α-(méthoxycarbonyl)-4-méthoxybenzyl]-2-phénylquinoléine-4-carboxamide ;
chlorhydrate de (R, S)-N-[α-(méthoxycarbonyl)-α-(méthyl)benzyl]-N-méthyl-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(2-hydroxyéthyl)benzyl]-2-phénylquinoléine-4-carboxamide ;
(-)-(S)-N-[α-éthylbenzyl)-5-méthyl-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(1-hydroxyéthyl)benzyl]-3-méthyl-2-phénylquinoléine-4-carboxamide ;
(R,S)-N-[α-(éthyl)-4-pyridylméthyl]-2-phénylquinoléine-4-carboxamide ;
(S)-N-(α-éthylbenzyl)-3-amino-5-méthyl-2-phénylquinoléine-4-carboxamide ; et
(S)-N-(α-éthylbenzyl)-3-méthoxy-5-méthyl-2-phénylquinoléine-4-carboxamide.

4. Procédé pour la préparation d'un composé de formule (I) suivant la revendication 1 ou la revendication 2, d'un composé suivant la revendication 3, ou d'un de ses produits de solvatation ou sels, qui comprend la réaction d'un composé de formule (III)



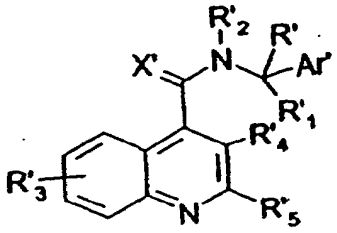
(III)

dans laquelle R', R'_1, R'_2 et Ar' représentent des groupes R, R_1, R_2 et Ar tels que définis par la formule (I) ou des groupes ou atomes pouvant être convertis en R, R_1, R_2 et Ar, avec un composé de formule (II)



(II)

ou un de ses dérivés actifs, formule dans laquelle R'_3, R'_4, R'_5 et X' représentent R_3, R_4, R_5 et X tels que définis pour la formule (I) ou des groupes pouvant être convertis en R_3, R_4, R_5 et X, pour former un composé de formule (Ic)



(Ic)

et ensuite, facultativement, la mise en oeuvre d'une ou plusieurs des étapes suivantes :

(a) lorsque R', R'_1 à R'_5, Ar' et X' sont autres que des groupes R, R_1 à R_5, Ar et X, la conversion de n'importe lequel des groupes R', R'_1 à R'_5, Ar' et X' en R, R_1 à R_5, Ar et X pour obtenir un composé de formule (I) ou un composé tel que défini dans la revendication 3,
(b) lorsque R', R'_1 à R'_5, Ar' et X' représentent des groupes R, R_1 à R_5, Ar et X, la conversion de n'importe lequel des groupes R, R_1 à R_5, Ar et X en un autre des groupes R, R_1 à R_5, Ar et X, pour obtenir un composé de formule (I) ou un composé tel que défini dans la revendication 3,
(c) la formation d'un sel et/ou d'un produit de solvatation du composé obtenu de formule (Ic) ou d'un composé tel que défini dans la revendication 3.

5. Procédé suivant la revendication 4, dans lequel le dérivé actif du composé de formule (II) est un halogénure d'acide.

6. Composition pharmaceutique comprenant un composé de formule (I) ou un de ses sels ou produits de solvatation, suivant la revendication 1 ou la revendication 2, et un support pharmaceutiquement acceptable.

7. Composition pharmaceutique comprenant un composé suivant la revendication 3 ou un de ses sels ou produits de solvatation, et un support pharmaceutiquement acceptable.

8. Composé de formule (I), ou un de ses produits de solvatation ou sels, suivant la revendication 1 ou la revendication 2, destiné à être utilisé comme substance thérapeutique active.

9. Composé suivant la revendication 3, ou un de ses sels ou produits de solvatation, destiné à être utilisé comme substance thérapeutique active.

10. Composé de formule (I), ou un de ses produits de solvatation ou sels, suivant la revendication 1 ou la revendication 2, destiné à être utilisé dans le traitement de troubles pulmonaires (asthme, maladies pulmonaires obstructrices chroniques -COPD-, hyperréactivité des voies aériennes, toux), de troubles cutanés et du prurit (par exemple, de la dermatite atopique et de la boule d'oedème et d'érythème cutanés), d'une inflammation neurogène et de troubles du SNC (maladie de Parkinson, troubles du mouvement, anxiété et psychose), de troubles convulsifs, de l'épilepsie, de troubles rénaux, de l'incontinence urinaire, d'une inflammation oculaire, d'une douleur inflammatoire, de troubles de l'alimentation (inhibition de l'absorption de nourriture), de la rhinite allergique, de troubles neuro-dégénératifs (par exemple la maladie d'Alzheimer), du psoriasis, de la maladie de Huntington et de la dépression.

11. Composé suivant la revendication 3, ou un de ses produits de solvatation ou sels, destiné à être utilisé dans le traitement de troubles pulmonaires (asthme, maladies pulmonaires obstructrices chroniques -COPD-, hyperréactivité des voies aériennes, toux), de troubles cutanés et du prurit (par exemple, de la dermatite atopique et de la boule d'oedème et d'érythème cutanés), d'une inflammation neurogène et de troubles du SNC (maladie de Parkinson, troubles du mouvement, anxiété et psychose), de troubles convulsifs, de l'épilepsie, de troubles rénaux, de l'incontinence urinaire, d'une inflammation oculaire, d'une douleur inflammatoire, de troubles de l'alimentation (inhibition de l'absorption de nourriture), de la rhinite allergique, de troubles neurodégénératifs (par exemple la maladie d'Alzheimer), du psoriasis, de la maladie de Huntington et de la dépression.

12. Utilisation d'un composé de formule (I), ou d'un de ses produits de solvatation ou sels, suivant la revendication 1 ou la revendication 2, dans la production d'un médicament destiné à être utilisé dans le traitement de troubles pulmonaires (asthme, maladies pulmonaires obstructrices chroniques -COPD-, hyperréactivité des voies aériennes, toux), de troubles cutanés et du prurit (par exemple, de la dermatite atopique, de la boule d'oedème et d'érythème cutanés), d'une inflammation neurogène et de troubles du SNC (maladie de Parkinson, troubles du mouvement, anxiété et psychose), de troubles convulsifs, de l'épilepsie, de troubles rénaux, de l'incontinence urinaire, d'une inflammation oculaire, d'une douleur inflammatoire, de troubles de l'alimentation (inhibition de l'absorption de nourriture), de la rhinite allergique, de troubles neurodégénératifs (par exemple la maladie d'Alzheimer), du psoriasis, de la maladie de Huntington et de la dépression.

13. Utilisation d'un composé suivant la revendication 3, ou d'un de ses produits de solvatation ou sels, dans la production d'un médicament destiné à être utilisé dans le traitement de troubles pulmonaires (asthme, maladies pulmonaires obstructrices chroniques -COPD-, hyperréactivité des voies aériennes, toux), de troubles cutanés et du prurit (par exemple, de la dermatite atopique, et de la boule d'oedème et d'érythème cutanés), d'une inflammation neurogène et de troubles du SNC (maladie de Parkinson, troubles du mouvement, anxiété et psychose), de troubles convulsifs, de l'épilepsie, de troubles rénaux, de l'incontinence urinaire, d'une inflammation oculaire, d'une douleur inflammatoire, de troubles de l'alimentation (inhibition de l'absorption de nourriture), de la rhinite allergique,

de troubles neurodégénératifs (par exemple la maladie d'Alzheimer), du psoriasis, de la maladie de Huntington et de la dépression.